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ADDRESSES AND ORIGINAL ARTICLES

THE BLOOD-BRAIN BARRIER IN INFECTIOUS DISEASES

ITS PERMEABILITY TO TOXINS IN RELATION TO THEIR ELECTRICAL CHARGES

BY ULRICH FRIEDEMANN, M.D. Berlin

LATE DIRECTOR OF THE INFECTIOUS DISEASES DEPARTMENT, RUDOLF VIRCHOW HOSPITAL, BERLIN; AND

A. ELKELES, M.D. Berlin.

LATE CHIEF ASSISTANT OF THE DEPARTMENT

1. Introduction: The Blood-brain Barrier

IN the pathogenesis of infectious diseases the brain is generally considered to be of outstanding importance. Symptoms characteristic of fevers, such as apathy, insomnia, delirium, raised temperature, vasomotor collapse, and eventually death, are ascribed to disturbances of the brain centres directly caused by bacterial toxins (H. H. Meyer and Gottlieb,[1] Wolff-Eisner [2]). This opinion appeared to be fairly reasonable as long as, according to Ehrlich, chemical affinities alone were supposed to control the relations between toxins and brain. Within the last few years, however, investigators have become aware of the existence of a selective mechanism regulating the exchange of substances between blood and brain. This mechanism has been described as "barrière hémato-encephalique" or "Bluthirnschranke." We propose to use the English equivalent and therefore shall speak of the blood-brain barrier or B.B.B. From all that is known about this barrier, and especially from our previous work, it has become very doubtful whether this barrier is passed by toxins. The investigation of this problem has been the main object of the researches dealt with in the first part of this paper.

It should be emphasised that this problem does not exactly coincide with the question as to whether toxins act on the brain, however closely both questions may be connected with one another. Tetanus toxin, for instance, does not pass the B.B.B., but acts on the brain and the spinal cord. On the other hand, non-susceptibility of the brain to toxins does not necessarily imply impermeability of the B.B.B. to the same toxins, because it may well be explained by lack of affinity to brain cells. This discrimination may appear somewhat irrelevant from the point of view of pathogenesis, but it is of great importance from its bearing on methods of investigation. Moreover, it is indispensable for the second part of the present paper, where the ability of toxins to pass the B.B.B. will be dealt with in connexion with their physico-chemical properties.

The methods available for the investigation of the selective mechanism of the B.B.B. have been described in a series of previous papers. Their application to the investigation of toxins and some modifications especially devised for this purpose will be discussed below. The experiments now described are largely confined to cobra venom and lamb-dysentery toxin, and a few have been made on botulinus toxin. In previous papers experiments on diphtheria toxin have been recorded. To arrive at more general conclusions it was necessary to include all information on the subject available from the literature. As a matter of fact the problem we are dealing with has hardly been ever discussed up to now, and the recorded experimental data have been largely misinterpreted. They are invaluable, however, when their real significance is recognised. The explanations we shall give of them are based on our previous experiments on the B.B.B. and differ considerably from those given by previous workers on toxins. A critical re-examination of the facts already recorded from this new aspect has therefore been an essential part of our work.

2. The Methods of Investigation of the B.B.B.

At the beginning of our experimental work no methods were available for the investigation of the selective mechanism of the B.B.B. The only method largely used by clinicians was the identification in the cerebro-spinal fluid of substances previously introduced into the body. This method was, however, based on completely erroneous conceptions of the localisation of the B.B.B.

According to Goldmann [3] and Lina Stern,[4] the B.B.B. was identified with the "Blutliquorschranke," the barrier localised in the choroid plexus and in the meningeal vessels; and substances circulating in the blood were supposed to reach the brain exclusively by way of the cerebro-spinal fluid. Walter [5] has shown, however, that this theory is incompatible with modern conceptions of brain metabolism. The oxygen consumption of the brain is now known to be very high, and the material necessary for combustion cannot be supplied by a fluid almost completely destitute of foodstuffs. The crucial experiments to refute Lina Stern's theory were carried out by Wesselkin,[6] Friedemann and Elkeles,[7] and Schmid [8] independently of one another. Friedemann and Elkeles found that alizarin blue and some basic aniline dyes, when injected intravenously, stain the brain but leave the cerebro-spinal fluid entirely uncoloured.

In accordance with Walter and Spatz we have come to the conclusion that, as regards the exchange of substances between blood and tissues, the brain does not materially differ from other organs. The selective mechanism of the B.B.B. is localised in the walls of the cerebral capillaries and coincides with the permeability of these vessels.

This result is fundamental to all methods described in the present paper. According to the character of the individual toxins a variety of methods has been devised. In some cases reliable results were obtained, only by the combined application of several methods. The individual methods will be described in detail in the following sections, but some general remarks may be made here. Action on the brain may generally be taken as indicating permeability of the B.B.B., unless there is some specific evidence to the contrary, as, for instance, in the case of tetanus toxin which will be discussed later, and can be demonstrated by physiological, pharmacological, and some other methods. On the other hand, permeability of the B.B.B. to toxins can be investigated independently of their action on the brain. For this purpose, after intravenous injection of the toxin, pieces of the brain emulsified in saline are introduced into other animals. Finally, action on the brain and permeability of the B.B.B. can be tested simultaneously by applying the methods of artificial perfusion of the brain, and of the auxoneurotropic effect. The combined application of several methods is necessary in those cases in which, under ordinary experimental conditions, the toxin has been shown to have no effect on the brain. In these cases the impermeability of the B.B.B. can be demonstrated in the following ways. Either the toxin can be shown to be effective when the B.B.B. is circumvented, or the absence of the toxin from the brain after its intravenous injection

can be demonstrated by the method described above. Only in the light of these fundamental considerations can facts recorded in the literature, as well as our own experiments, be interpreted accurately. The lack of a clear understanding of methods will be found to be responsible for the misinterpretations with which we shall meet in reassessing the significance of recorded facts. After these general remarks we now proceed to a more detailed discussion of the individual toxins.

3. Permeability of the B.B.B. to Toxins

UNIDENTIFIED TOXINS OR ENDOTOXINS CAUSING GENERAL FEVER SYMPTOMS

Bacterial toxins prepared in artificial media and studied experimentally are few in number. Yet the opinion is prevalent that symptoms common to all fevers such as raised temperatures, apathy, insomnia, delirium, and metabolic disturbances are directly caused by toxic substances of bacterial origin. Although no experimental evidence whatsoever is available to support this opinion, yet it is chiefly responsible for the general conception that toxins act on the brain. As a matter of fact clinical observations are very unreliable in ascertaining the cerebral origin of pathological disturbances. The brain centres regulating temperature, blood pressure, and metabolism control very complicated peripheral mechanisms, and the conception that disturbances in the functions controlled by these centres are caused by lesions of the centres themselves is largely hypothetical. Cramer,[9] for instance, pointed out that in the production of fever the thyroid gland and the suprarenals have an important part. As a rule, it is also not sufficiently realised that infection produces a series of severe changes in metabolism and in the physical condition of the body which may lead to cerebral symptoms. There are some experimental indications that raised temperature in fevers may be partially due to these secondary conditions. When fresh guinea-pig serum is incubated with dead bacteria or with agar (Bordet [10]) or starch (Nathan [11]) it acquires pyrogenic properties (Friedberger and Mita [12]). These observations strongly suggest that, under the influence of infection, pyrogenic substances are produced in the blood and in the tissues. On the other hand, there are indications that raised temperature or metabolic processes connected with it may produce cerebral symptoms characteristic of infectious fevers. We cannot but accept this explanation for the well-known fact that in typhoid fever pyramidon frequently removes all these symptons, although it certainly does not neutralise toxins.

This is all we know of these unidentified toxins. We emphasise the fact that common fever symptoms have not been proved as yet to be directly caused by the action of bacterial toxins on brain centres. No evidence whatsoever is available as regards the question whether or not these toxins pass the B.B.B.

DIPHTHERIA TOXIN

Of all toxins diphtheria toxin has been most thoroughly investigated. Meyer and Gottlieb merely express the current opinion in saying that death in diphtheria is due to poisoning of brain centres. From a clinical point of view this assertion, however, is not convincing. In diphtheria, in particular, cerebral symptoms characteristic of other febrile diseases such as apathy, insomnia, and delirium, are not observed. Fever is frequently absent in the most severe cases, and the respiratory centre is hardly ever involved.

The opinion of Meyer and Gottlieb is mainly based on the conception of Romberg and Pässler [13] that death in diphtheria is due to failure of the vasomotor centre. This conception, however, although nearly unanimously accepted, cannot be maintained any longer. Vasomotor collapse, indeed, has been shown by MacCallum [14] to be an outstanding factor in diphtheria poisoning. But Porter and Pratt [15] found that the vasomotor centre is not at all impaired in experimental diphtheria, not even in the final stages of the disease. To us these two facts can be explained only under the assumption that vasomotor collapse in diphtheria is of peripheral origin and cannot be regarded as a proof for the cerebral action of diphtheria toxin.

Caporali [16] and Speransky [17] claimed to have proved by indirect methods that death in diphtheria is brought about by an action of the toxin on the brain. Caporali injected rabbits intravenously with diphtheria toxin and compared the effects of antitoxin by the intracerebral and the intravenous route. He found that antitoxin was more effective when given intracerebrally. Speransky stated that in rabbits the power of antitoxin is enhanced by repeated withdrawal and reinjection of cerebro-spinal fluid, a process by which, he claimed, an increased permeability of the choroid plexus is induced. If these experimental results are accepted, it must be regarded as demonstrated that diphtheria toxin has a direct action on the brain. Friedemann and Elkeles,[18] however, in a large series of experiments, failed to confirm the results of Caporali and Speransky.

Another series of Caporali's experiments are very instructive in that they show that a misinterpretation of the experimental evidence becomes inevitable when the mechanism of the B.B.B. is ignored. Caporali claimed to have demonstrated the importance of the brain in the pathogenesis of diphtheria by the fact that diphtheria toxin when injected intracerebrally is 10 to 20 times more effective than by the intravenous route. This fact, however, although confirmed by Friedemann and Elkeles, only reveals the high toxicity of diphtheria toxin to brain cells when the B.B.B. is circumvented. It does not imply that diphtheria toxin has any effect on the brain when introduced in the ordinary way. But the affinity of diphtheria toxin to brain cells demonstrated by Caporali's experiments clearly shows that the inactivity of diphtheria toxin on brain, demonstrated by Porter's and Pratt's experiments, can only be explained by the impermeability of the B.B.B. to the toxin. The correctness of this explanation is shown by the following experiments which again were not interpreted in this way at the time when they were carried out.

As early as 1898 Roux and Borrel [19] have found that diphtheria toxin is almost innocuous to the rat when given by the ordinary routes. Injected intracerebrally, however, it proved to be as toxic as in the most susceptible animals. From our point of view the experiment can be explained only by the assumption that, at least in the rat, the B.B.B. is completely impermeable to diphtheria toxin.

Final proof for this conclusion can be found in the experiments of Bieling and Gottschalk,[20] who tried to identify diphtheria toxin in the various organs of animals which had received toxin intravenously. They succeeded in finding it in most organs, but they entirely failed to find it in the brain. These experiments were repeated by Friedemann and Elkeles [18] with exceedingly high amounts of toxin, and with identical results.

When all the experimental evidence is taken together it is clear that, contrary to an opinion hitherto believed to be well founded, diphtheria toxin does not act on the brain in the acute stage of the disease, because it cannot pass the B.B.B.

The opinion that diphtheria toxin is poisonous to the central nervous system was also suggested by the appearance of paralysis in the late stages of the disease. In a very careful histological study Pierre Uhry [21] recently arrived at the conclusion that lesions are only found in the peripheral nerves. We think that this result presents a satisfactory explanation for the complete curability of post-diphtheric paralysis. In poliomyelitis, where the cells of the brain and of

the spinal cord degenerate and die, permanent paralysis, as a rule, remains after the disease itself has subsided.

BOTULINUS TOXIN

Another toxin which is generally regarded as a specific toxin for the central nervous system is botulinus toxin. This opinion was even held by Forssman [22] although his experiments, in our opinion, prove exactly the reverse. While Kempner and Pollak,[23] Ossipoff,[24] and Römer and Stein [25] believe that they have found definite histological changes in the ganglion cells of the brain and of the spinal cord, Dickson and Shevky, in a very careful investigation, completely fail to confirm these results. As an outcome of their own experiments they conclude that botulinus toxin acts on the peripheral nerves. They found that in the parasympathetic nervous system the conduction of the nerve impulses is blocked by the toxin. The motor nerves were shown to have become susceptible to abnormally rapid fatigue on faradic irritation.

The most striking proof for the peripheral action of botulinus toxin, at least as we see it, was afforded by Forssman's experiments. No increased toxicity was observed when the toxin was introduced intracerebrally. Moreover, under these conditions, the toxin was easily neutralised by antitoxin given in the ordinary way. From all we know, these results are completely incompatible with the assumption that botulinus toxin has any specific affinity for brain cells. On the other hand, a special effect of the toxin on the action of the diaphragm could be demonstrated. The lethal dose was considerably reduced when the toxin was introduced into the lungs, the pleural or the peritoneal cavity, and under these conditions the diaphragm was paralysed. Antitoxin was ineffective as soon as symptoms had appeared.

Keeping in mind the lack of affinity of the toxin for brain cells, made evident by the above experiments, we could not expect an effect on the brain, even when the B.B.B. was permeable to the toxin. It was necessary, therefore, to investigate this question separately, by a method independent of the affinity of the toxin for brain cells.

With this object the following experiments were carried out.

Botulinus toxin A, which was kindly placed at our disposal by Prof. H. Schmidt, Marburg, and of which 0·00005 c.cm. injected intraperitoneally killed mice within 48 hours, was injected intravenously into mice. 0·1 c.cm. was used. After one hour the mice were killed and the toxin contents of brain and blood were compared. The results were not quite consistent. In the majority of the experiments the brain was completely free from toxin. In one experiment some toxin was found in the brain. But the amount was so insignificant, as compared with that of the blood, that we are inclined to ascribe it to the blood content of the brain. As a characteristic example the following experiment is described in detail.

A mouse of 20 g. had 0·1 c.cm. botulinus toxin A injected intravenously. The mouse was killed after one hour and the brain (400 mg.) ground in 1 c.cm. saline. 0·25 c.cm. of this emulsion injected intraperitoneally into a mouse of 20 g. was innocuous. 0·0001 c.cm. blood, also injected intraperitoneally, killed the mouse within 24 hours.

This experiment shows conclusively that the B.B.B. is impermeable to botulinus toxin.

TETANUS TOXIN

In a number of ways and by a number of investigators tetanus toxin has been conclusively proved to act upon the central nervous system, but it was early realised that tetanus toxin does not pass directly from the blood to the spinal cord; it reaches the central nervous system by way of the peripheral nerves. Two fundamental facts are the basis of this conception. First, the orderly inter-relation between the length of the incubation in the individual species and their relative size. Secondly, the beginning of symptoms in the site where the toxin has been injected. Moreover, Meyer and Ransom [27] could directly identify in the sciatic nerve the toxin previously injected subcutaneously into the hind leg of a cat. In this way they clearly demonstrated the wandering of the toxin in the peripheral nerves. Another set of ingenious experiments were carried out by Meyer and Ransom to the same purpose. They are not, however, dealt with in detail, because they have considerably lost in credit, since Horster and Whitman [28] have shown, in experiments with dyes, that toxin and antitoxin injected into the sciatic nerve apparently reach the spinal cord at once. There remains, however, sufficient evidence for the conception that the toxin reaches the spinal cord and the brain exclusively by way of the peripheral nerves. In our opinion this fact can only be explained by the assumption that the B.B.B. is completely impermeable to tetanus toxin.

THE TOXINS OF VIBRION NASIK AND VIBRION EL-TOR

In this and in the following sections a group of toxins will be considered which differ from the majority of toxins in the lack of an incubation period, and the rapidity of their action. We begin with the toxins of vibrion Nasik and vibrion El-Tor.

The mechanism of their action was carefully studied by Rothberger.[29] 3 to 5 c.cm. injected intravenously kill rabbits within two minutes. Injected in smaller doses they produce characteristic symptoms of dyspnœa. Rothberger attributes, however, no significance to these symptoms, on account of the fact that artificial respiration did not prevent or even delay death. He ascribes death to heart failure, demonstrated in the isolated heart of the cat, and feels entitled to deny any action of the toxins on the brain. In our opinion this conclusion is not warranted. The symptoms of dyspnœa observed by Rothberger seem to indicate that, in addition to heart failure, the respiratory centre is severely poisoned.

Unfortunately we have had no opportunity to apply the methods described below to the toxins of vibrion Nasik and vibrion El-Tor. The question whether they pass the B.B.B. therefore remains open, but we are rather inclined to answer it in the affirmative.

LAMB DYSENTERY TOXIN

The lamb dysentery bacillus was isolated by Gaiger and Dalling [30] in O'Brien's laboratory during an epidemic in newly born lambs. It is an anaerobic micro-organism of the perfringens group. The toxin was also discovered by Gaiger and Dalling, and a dried sample of it kindly placed at our disposal by Dr. O'Brien. It is a most powerful toxin which, injected intravenously, kills mice, guinea-pigs, and rabbits in doses of some miligrammes, and in a few minutes.

The toxins of other gas œdema bacilli resemble lamb-dysentery toxin in the rapidity of their action. The mechanism of this action was investigated by Miss Robertson [31] in the toxin of vibrion septique and by Straub [32] in the toxin of the "Gasbrand-bacillus of Ficker." Both authors demonstrated an acute action on the heart. As far as we are aware the mechanism of the action of lamb-dysentery toxin has not yet been investigated. We therefore record some interesting observations we met with in our experiments. There is a peculiar action on the heart. The auricles continue their activity after the ventricles have stopped beating. It would

be interesting to find out whether this dissociation between auricles and ventricles is due to heart-block.

An action on peripheral nerves could be demonstrated in the following way. The sciatic nerves of a rabbit were exposed on both sides. On the right side the nerve was brushed with a solution of the toxin, on the left side with saline. Half an hour later a paralysis of the right leg set in and lasted for three days until death occurred. The left leg remained unaltered during the course of the experiment. The peripheral action of lamb-dysentery toxin is evident from this. Whether in addition to it the brain is involved was investigated by the following experiments.

The methods of the artificial perfusion of the brain and of the auxoneurotropic effect described below can be applied only to toxins which exhibit an affinity to brain cells. Before applying these complicated methods it appeared reasonable therefore to make sure that this condition was fulfilled. To this effect in a series of rabbits of 2500 g. the lethal dose of lamb-dysentery toxin was determined by the intravenous route, in another series by the intrathecal route.

TABLE I

Dose of lamb-dysentery toxin.	Rabbits which received the dose of toxin—	
	Intravenously.	Intrathecally.
100 mg. ..	+ 2 mins. after injection.	..
20 mg. ..	..	+ some hrs. after injection.
10 mg. ..	+ 5 mins. after injection.	+ some hrs. after injection.
5 mg. ..	+ 4 mins. after injection.	..
4 mg. ..	+ 5 mins. after injection.	..
2 mg. ..	+12 mins. after injection.	+ some hrs. after injection.
1 mg. ..	+27 mins. after injection.	+ some hrs. after injection.
1 mg. ..	Survived.	
0·5 mg. ..	,,	+ some hrs. after injection. Survived.
0·25 mg. ..	..	

It will be seen from these experiments (Table I.) that the lethal dose in the intrathecal is nearly four times lower than in the intravenous route. This result can only be explained by an affinity of lamb-dysentery toxin to brain cells. In spite of this increased toxicity the action is considerably delayed in the intrathecal route. Apparently diffusion through cerebral tissue is rather slow. Having demonstrated in this way the affinity of the toxin to brain, it was now necessary to determine whether the B.B.B. is permeable.

The method of the artificial perfusion of the brain was described by us in a previous paper.[32] It bears a close resemblance to the method of cross perfusion of the brain invented by Frédéricq[34] and Gaskell and Shore.[35] The brain of a rabbit, the receiver, is perfused by the blood of another rabbit,* the donor, by linking the carotids and jugular veins of both animals. The subclavian arteries of the receiver are ligatured near to their origin. Using alizarin blue as an indicator we were able to show that no perfusion at all is observed when the subclavian arteries are not ligatured. Blood clotting is prevented by the intravenous injection of heparin, generously placed at our disposal by the Schering A.G.

It is well known that in the dog the circulation of the brain cannot be completely separated from the general circulation on account of some anastomoses between the vertebral and the anterior spinal arteries.[36] But it is generally held that these anastomoses are insignificant in rabbits. This is, however, not quite true. In previous experiments we had pointed out indeed that alcohol, urethane, somnifen, and luminal natrium when injected into the femoral vein of the receiver left the brain entirely unaffected. Paraldehyde, however, under the same conditions abolished the brain reflexes of the receiver.[33] The different action of the various narcotics is probably explained by a different action on blood-vessels, and consequently on the anastomoses between vertebral and anterior spinal arteries. Special stress is laid upon this observation, because it proved to be very helpful in the course of our experiments with lamb-dysentery toxin.

In the first series of experiments the toxin was injected into the brain circulation of the receiver. For this purpose some modifications of our original method were necessary. Obviously the donor would be killed, and the brain circulation immediately stopped, if the blood containing the toxin were allowed to return to the donor. The jugular veins of the receiver, therefore, were not linked with those of the donor. The blood was allowed to pour freely from the jugular veins of the receiver. To replace the loss of blood an appropriate amount of normal rabbit blood was intravenously introduced into the donor. The toxin was injected into the brain circulation of the receiver —i.e., into the carotids. Although a large series of experiments was carried out the results were unsatisfactory. In fact, the brain reflexes of the receiver (corneal, lip, tongue reflexes) disappeared three to five minutes after the injection of the toxin. But at the same time the brain circulation became insufficient. Apparently the blood-supply to the donor could not balance long enough the inevitable loss of blood.

In a second series of experiments the toxin was injected into the femoral vein of the receiver. The original method of perfusion was used. The peripheral action of the toxin was demonstrated clearly. The spinal reflexes disappeared, and the ventricles stopped beating. But, in the majority of experiments, the brain reflexes also disappeared three to five minutes after injection of the toxin, although the brain circulation was still excellent. Apparently the toxin reached the brain by way of the anastomoses between the vertebral and anterior spinal arteries. By these experiments the action of lamb-dysentery toxin on brain and the permeability of the B.B.B. to the toxin are clearly demonstrated.

These results are confirmed by the method of the auxoneurotropic effect. This phenomenon was described by us in a previous paper,[37] but as a method of testing the permeability of the B.B.B. it was used for the first time in these experiments. We found that the permeability of the B.B.B. is considerably increased both by adrenaline and pituitrin. This increase of permeability, however, is to some extent selective. It concerns exclusively those substances which normally pass the B.B.B. The efficiency of narcotic drugs and strychnine was increased to from five to ten times its normal value on account of the increased permeability of the cerebral vessels. On the contrary the latter was found not to be increased for trypan-blue, salvarsan, and cobra antitoxin, which normally do not pass the B.B.B. The demonstration of the auxoneurotropic effect therefore indicates that the substance under investigation passes the B.B.B. and acts on the brain.

Using alizarin blue S as an indicator we could clearly demonstrate that the phenomena described above must be explained by an increased permeability of the cerebral vessels. To stain the brain definitely 10 to 15 c.cm. of a 5 per cent. solution of alizarin blue S must be introduced intravenously. When 2 to 3 c.cm. of adrenaline solution 1–10,000 are given previously, 2 c.cm. of the same alizarin blue solution effect an intense staining of the brain, the lungs, and the heart. Obviously the permeability of the vascular system is increased in all those areas which do not participate in the general vasoconstriction produced by adrenaline. This suggests that the phenomenon is due, partly at any rate, to the rise in blood pressure. In the pulmonary vessels the increased permeability eventually results in lung œdema (Lusiada).[38] Pituitrin has an antagonistic effect on the pulmonary vessels. When adrenaline and pituitrin are given simultaneously, no lung œdema is observed and the lungs remain unstained. In a series of hitherto unpublished experiments we found that in this respect Hypophysine of the I.G. Farben A.G. (1 c.cm.=3 international units) gave the best results. Pituitrin, Pitressin, and Pitocin of Parke Davis were far less effective. We have the impres-

* The experiments on cross-perfusion were all carried out at the Rudolf Virchow Krankenhaus, Berlin.

sion that, apart from the vasopressin and the oxytocin, there is a third component in the posterior lobe of the pituitary gland which specifically affects the pulmonary vessels. An action of pituitrin or hypophysine on the coronary arteries, suggested by some pharmacological observations, could not be clearly demonstrated as yet by the alizarin blue method. The cerebral vessels remain completely unaffected by pituitrin or hypophysine. The brain is even more intensely stained when hypophysine is added to adrenaline. We infer from these experiments that the combined application of adrenaline and hypophysine effects a fairly specific increase of the permeability of the cerebral vessels. In our experiments with lamb dysentery toxin 1 c.cm. hypophysine of the I.G. Farbenindustrie A.G. (1 c.cm.=3 international units) was injected intravenously. One minute later 2–3 c.cm. adrenaline, 1–10,000, and immediately afterwards various doses of lamb-dysentery toxin were introduced, both of them intravenously.

TABLE II

Dose of lamb-dysentery toxin.	Controls—rabbits which had received no hypophysine and no adrenaline.	Rabbits which had received 1·0 c.cm. hypophysine then 0·3 mg. adrenaline.
2·0 mg. ..	+ 10 mins. after injection.	..
1·0 mg. ..	+ 19 mins. after injection.	..
0·5 mg. ..	Survived.	+ 11 mins. after injection.
0·25 mg. ..	..	+ 24 hrs. after injection.

As a result of these experiments (Table II.) we found that by hypophysine and adrenaline the toxicity of lamb-dysentery toxin is considerably increased. It amounts to four times its original value. These experiments, as well as those in which the perfusion method was used, show conclusively that the B.B.B. is permeable to lamb-dysentery toxin.

COBRA VENOM

Cobra venom was chosen as a representative of animal toxins. The venoms of the crotalus group were inappropriate for our purpose on account of their hæmorrhagic components, which were expected to change the permeability of the B.B.B. We are deeply indebted to Dr. Th. Madsen, Copenhagen, for a large sample of dried cobra venom with which the following experiments were carried out.

A very careful investigation on the mechanism of cobra venom poisoning was made by Elliot.[39] A peripheral action of cobra venom was clearly demonstrated. Constriction of the arterioles of the frog's leg was produced by perfusing it with a 1 : 10,000,000 solution of the toxin. The hearts of frogs and mammals stopped beating when perfused with 1 : 500,000 solutions. Heart failure was prevalent in animals when large doses were given; but with small doses respiratory disturbances were observed. On account of these disturbances Elliot took the cerebral effect of cobra venom for granted. According to Arthus,[40] however, the nerve-endings in the diaphragm are paralysed by cobra venom.

In our own experiments the methods described in the preceding section were used. The results of the comparative intravenous and intrathecal injections are shown in Table III.

The intrathecal is at least ten times more effective than the intravenous injection. This means that cobra venom has a strong affinity to brain cells. Here again, as in the experiments with lamb-dysentery toxin, death was considerably delayed in the experiments with intrathecal injection on account of the slow diffusion of cobra venom through brain tissues. It is noteworthy that the results of the intravenous and intrathecal methods differ far more with cobra venom than with lamb dysentery toxin. Apparently cobra venom is more toxic to brain cells than lamb-dysentery toxin.

TABLE III

Dose of cobra venom.	Rabbits which received the dose of toxin—	
	Intravenously.	Intrathecally.
10 mg. ..	+ 3 mins. after injection.	..
5 mg. ..	+ 6–9 mins. after injection.	..
2·5 mg. ..	+ some hrs. after injection.	..
1·7 mg. ..	+ some hrs. after injection.	..
1·0 mg. ..	Survived.	+ 25 mins. after injection.
0·4 mg. ..	..	+ some hrs. after injection.
0·3 mg. ..	..	+ some hrs. after injection.
0·2 mg. ..	..	+ some hrs. after injection.

In applying the perfusion method we met with an unexpected complication. When cobra venom was injected into the brain circulation of the receiver the brain reflexes disappeared immediately and convulsions set in. But at the same time the outflow of blood from the jugular veins of the receiver stopped at once. This phenomenon is apparently due to constriction of the brain vessels. At least this explanation is suggested by Elliot's experiments. This vasoconstriction is the reason why the perfusion experiments gave no information on the permeability of the B.B.B. to cobra venom. When cobra venom was injected into the femoral vein of the receiver the spinal reflexes disappeared at once and the heart stopped beating. The peripheral action of cobra venom could be demonstrated, which has already been shown by Elliot with other methods. The brain reflexes remained uninfluenced for 20 minutes. Lamb-dysentery toxin and cobra venom differ from one another very much in the same way as has been described above for paraldehyde and the other narcotics. Apparently the anastomoses between the vertebral and anterior spinal arteries are constricted by cobra venom.

The auxoneurotropic effect on cobra venom is shown in Table IV. :—

TABLE IV

Dose of cobra venom.	Controls—rabbits which had received no hypophysine and no adrenaline.	Rabbits which had received 1·0 c.cm. hypophysine and 0·3 mg. adrenaline.
2·0 mg. ..	+ 5 mins. after injection.	..
1·0 mg. ..	+ 18 mins. after injection.	..
0·5 mg. ..	+ 40 mins. after injection.	..
0·1 mg. ..	..	..
0·05 mg. ..	..	+ 4 mins. after injection.
		+ 10 mins. after injection.

The toxicity of cobra venom is increased to as much as 20 times its normal value by hypophysine and adrenaline. The permeability of the B.B.B. to cobra venom is made clear by these experiments. The auxoneurotropic effect is much stronger with cobra venom than with lamb-dysentery toxin. Evidently cobra venom is more toxic to the brain. The experiments therefore confirm the conclusion arrived at by a comparison of the intravenous and the intrathecal routes. As a whole, our experiments as well as those of Elliot suggest that the B.B.B. is permeable to cobra toxin.

4. Summary of the Preceding Investigations

We have thus reached a point at which, from experiments of our own and from a critical review of observations gathered from the literature, it can be stated that toxins differ among themselves in the facility with which they pass the blood-brain barrier. We can say that, of the seven toxins upon which information is available, two—viz., lamb-dysentery

toxin and cobra venom—pass the B.B.B. The toxins of the vibrion Nasik and vibrion El-Tor are not yet sufficiently known in this respect. There are some indications that they too pass the B.B.B. Three toxins, those of tetanus, diphtheria, and botulinus, are definitely proved not to pass the B.B.B.

There is another quality according to which the toxins under investigation fall into the same groups as according to their ability to pass the B.B.B. All toxins which were shown to pass the B.B.B. are characterised by the lack of an incubation period and the rapidity of their action. The toxins which do not pass follow the rule that the incubation period of toxins is commonly a long one. In the following section we shall record new facts which strongly suggest that this coincidence is more than accidental. If this is conclusively proved, it would mean that the majority of toxins do not pass the B.B.B. We still avoid, however, a generalisation like this. We are satisfied to point to the result that two toxins—viz., diphtheria and botulinus toxin—which hitherto have almost unanimously been believed to act on the brain, in reality have no effect on it. This is a most important result with regard to the pathogenesis of infectious diseases, and we shall have to refer to it again in the discussion.

(To be concluded)

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THE TOXÆMIA OF ACUTE INTESTINAL OBSTRUCTION

THE VALUE OF B. WELCHII ANTITOXIN IN ITS TREATMENT

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It is doubtful whether any subject has attracted wider attention or resulted in more extensive investigation than has acute intestinal obstruction. The interesting and varied nature of the problem, together with the persistently high mortality resulting from the recognised lines of treatment, has provided a constant stimulus to research and a keen search for the so-called toxin of acute obstruction.

The existence of very toxic substances in the stagnant contents of obstructed loops of intestine was proved many years ago.[1] These substances when injected intravenously or intraperitoneally quickly cause death. Similar substances were shown later to be present in the contents of normal intestine,[2 3] especially after a protein meal.[4] It is well known that during normal digestion the intestinal mucosa displays a selective power in that substances of large molecular structure are not absorbed. Experiments by Wilkie [5] and others,[6 7] proving that the normal mucosa of the small intestine prevented the absorption of the products of intestinal putrefaction in appreciable quantity, dealt a severe blow to the generally accepted belief in the presence of a single lethal factor which accounted for death in all types of acute obstruction.

Hartwell and his co-workers[8] were the first to bring forward the theory that toxæmia in acute obstruction did not make its appearance in the presence of uninjured mucosa. They examined all the experimental data of Whipple and his associates and found that, in every case in which death supervened with obstruction or a closed loop, there were gross changes in the mucosa. Brooks[9] agreed with Hartwell that the toxæmia is directly proportional to the injury to the mucosa, and stated that the changes in the mucosa are caused largely by distension of the gut and the resulting embarrassment of the circulation. He added that there are two factors in the development of the toxæmia of obstruction, firstly the elaboration of the toxin, and secondly opportunities for the absorption of the toxin; and of these he believed the latter to be more important.

ELABORATION AND ABSORPTION OF THE TOXIN

The bacterial origin of the toxins in the content of obstructed bowel is now generally accepted. Those who tried to ascertain the rôle played by bacteria were faced with the almost insuperable difficulty of eliminating them entirely from segments of intestine. However, Dragstedt and his co-workers[10] isolated segments of intestine and left them open in the peritoneal cavity with all the nerves and vascular elements intact. At a later date another laparotomy was done and the loop contents found to be sterile. The ends of the loop were then inverted and the closed sterile loops returned to the abdomen. They found that animals so treated lived indefinitely, and furthermore they were able to strangulate these loops without any deleterious effect. Murphy and Brooks[11] carried out similar experiments and obtained the same results. The conclusion is that bacteria are necessary for the production of the toxin.

A toxæmia, that is to say a condition resulting from the absorption of toxic substances from the obstructed intestine, is not present in all cases of acute intestinal obstruction. It depends on the presence of a severely damaged mucosa in the obstructed segment. The importance of this factor of mucosal damage is evident in the recognition of three distinctive types of obstruction. These are :—

1. *Simple obstruction*, by which is meant an occlusion of the intestinal lumen not complicated by a circulatory disturbance of the obstructed segment of intestine.

2. *Acute strangulation*, in which the obstructing mechanism interferes grossly with the circulation of the obstructed loop, usually affecting the vessels in the mesentery.

3. *Distension necrosis*, in which the progressive distension of the obstructed segment (whether open or closed) interferes with the circulation of the intestinal wall and produces patchy gangrene of the mucosa.

In simple obstruction the excessive vomiting, which is such a marked feature of these cases, results in a progressive dehydration and sodium chloride loss with ultimate death. The most persuasive evidence that dehydration can be a directly fatal condition is the fact that death can be prevented and symptoms removed if the dehydration is adequately repaired by the subcutaneous or intravenous administration of sufficient quantities of the lost material in the form of a physiological sodium chloride solution. Gamble and his co-workers [12] state that this simple explanation is sufficiently indicated by the data at hand to make unnecessary the hypothesis of a toxin absorbed from the gastro-intestinal tract.

The other two conditions present a very different pathology. In acute strangulation, as it is seen clinically, the veins draining the loop are obstructed and the arteries remain patent, with the result that the loop becomes increasingly distended with blood until thrombosis closes the smaller arteries. Under such conditions the cause of death depends on the length of bowel involved.[13] When long loops (two feet or more) are affected, sufficient blood is withheld from the circulation by the loop to produce an acute circulatory collapse and death. Moderate-sized loops (one to two feet) are unable to hold up sufficient blood in this manner, and in these cases it has been shown that death is due to the absorption from the peritoneal cavity of the fluid exuding from the loop. This fluid is at first indistinguishable from blood plasma, but about 16 hours after the onset it begins to contain toxic substances in increasing quantity which result from the action of bacteria on the disintegrating tissues of the intestinal wall. When short loops (less than one foot) are strangulated, the process goes a step further and death is preceded by a perforation of the loop which floods the peritoneum with a toxic fluid which is also swarming with bacteria, and death results from a combination of toxæmia and peritonitis.

Distension necrosis is always the result of delay in relieving the obstruction. Most cases begin either as a simple obstruction or as an obstructed loop in which primarily there is no interference with the circulation of the obstructed intestine. As a result of delay in treatment, and aggravated by the use of purgatives and the taking of drinks, the intestine becomes progressively distended. The effect of such distension is most marked in that portion of the bowel furthest removed from its mesentery, and capillary rupture with submucous hæmorrhages results.[14] The mucosa is damaged and the contents of the intestinal lumen come into direct contact with the unprotected tissues of the intestinal wall and death may follow from the absorption of toxic substances from the lumen. But while these changes are taking place the patient is frequently vomiting and the resulting dehydration may become a serious factor. In this way distension necrosis combines the features of simple obstruction and strangulation.

Toxæmia therefore only occurs in those cases of acute obstruction where the wall has been sufficiently damaged to allow of abnormal absorption, and this factor, rather than the mere presence of the toxins in the lumen, is evidently the dominant one. The exact nature of the toxin of acute intestinal obstruction is unknown, and this adds to the experimental difficulties experienced in producing evidence of the absorption of a toxin from the obstructed intestine. In acute strangulation it has been conclusively shown that the prevention of absorption via the peritoneal cavity by enclosing the strangulated loop in a rubber bag will materially prolong the life of animals.[13] The direct evidence of the presence of a toxin in the blood of animals dying of distension necrosis is very scanty. Sugito [15] aspirated blood from the veins in the mesentery of an obstructed loop and found that the serum obtained from this blood was toxic to mice, and although Scholefield [16] corroborated these observations he emphasised the fact that the blood must be obtained during the last few moments of life to show toxicity. In consequence of the difficulty of obtaining direct evidence of the absorption of toxins from obstructed loops, the problem has been studied by indirect methods. One of the most important of these has been the study of the part played by the *Bacillus welchii* in the pathology of acute intestinal obstruction.

THE B. WELCHII THEORY

The nature of the bacteria responsible for the elaboration of the toxin did not arouse great attention until the publication in 1926 of a paper by Williams,[17] who advanced the hypothesis that the toxæmia of acute obstruction was due at least in part to the absorption of the toxin of *B. welchii* from the obstructed bowel. He noted the marked resemblance of the terminal stages of the toxæmia of gas gangrene to that of acute obstruction. He observed that *B. welchii* was by far the commonest anaerobe in the intestinal tract, and he isolated it from the vomitus and intestinal content after obstruction in a high percentage of cases of ileus. On the basis of this theory he gave *B. welchii* antitoxin to patients suffering from intestinal obstruction or peritonitis with an apparently favourable effect upon the mortality-rate. The suggestion that the toxæmia of acute intestinal obstruction is due to a known bacterial toxin aroused considerable interest, especially since the effects of the toxin suggested could be counteracted by a specific antitoxin. Numerous papers on the subject have since been published and I shall summarise them briefly.

Morton and Stabins [18] found that in dogs the development of the toxæmia following obstruction in the jejunum seemed to be delayed by the administration of the antitoxin, and the mortality was lower in an mals given the antitoxin before operative relief. Owings and McIntosh [19] concluded that the life of dogs with high intestinal obstruction was not prolonged by the use of *B. welchii* antitoxin. It is unfortunate that these experiments have dealt with high obstruction only, in which there is no evidence to show that a toxæmia ever exists. In these cases the main lethal factor is dehydration and not toxæmia, and therefore the value of *B. welchii* antitoxin cannot be decided on such experiments.

The number of workers who have studied the value of *B. welchii* antitoxin in the type of case in which

toxæmia is known to exist is not very large. In 1929 McIver, White, and Lawson [20] selected for their experiments a closed loop of bowel, the veins of which were ligated, producing an acute strangulation. They gave their reasons for choosing this type of obstruction as follows. Firstly, death is known to be due to a toxæmia; secondly, death occurs before water and chloride loss can affect the issue; and thirdly, the conditions existing in a strangulated loop have been shown to be ideal for the growth of anaerobic bacteria. The experiment was therefore well planned but they were unable to show that the administration of *B. welchii* antitoxin prolonged the life of their animals. The only criticism which may be levelled at their experiments is that they were putting *B. welchii* antitoxin to the severest possible test. Perforation of a strangulated loop and flooding of the peritoneum with a highly toxic and infected fluid is the rule about 24 hours after the onset of strangulation. It is unlikely that any systemic treatment can affect the issue in such cases.

Copher, Stone, and Hildreth [21] utilised an isolated closed loop of jejunum and stated that the administration of *B. welchii* antitoxin on the day of operation prolonged the lives of their animals. Thurston [22] carried out a similar series. He stated that:

> The production of a closed loop is a questionable procedure because rupture of the loop with peritonitis is so commonly found after death, to which, of course, no immunity is possible. If the loop is found intact and no other cause for death is found, it is reasonable to assume that absorption of some of the lethal bodies within the loop has caused death. In animals with unruptured loops and without simple obstruction the administration of the specific antitoxin should have prolonged life if the absorption of that particular toxin is the cause of death.

He concluded from his experiments that the *B. welchii* antitoxin had neither a prophylactic nor a therapeutic value.

The ideal case in which to test the value of *B. welchii* antitoxin is undoubtedly an obstruction situated in the lower ileum or colon. Such cases usually terminate in the condition described as distension necrosis, and death is due to the absorption of a toxin from the obstructed segment. There is no complicating peritonitis, and if *B. welchii* toxin plays any part in the toxæmia of acute obstruction it is in this type of case that the antitoxin should prove its value. These cases present the added attraction of occurring very frequently in clinical practice. North [23] selected an obstruction of the terminal ileum for his experiments. He stated that the use of *B. welchii* both intravenously and enterally does not provide any evidence that it exerts a deterrent influence upon toxæmia or prolongs life following the production of a low intestinal obstruction closely simulating that encountered by the surgeon. He added that giving the antitoxin in a single dose at the time of operation, as he did, might not render it available at the time it was most needed. When discussing low obstruction in dogs, he stated that the changes in the blood chemistry are inconspicuous and that vomiting does not occur. He accordingly did not administer sodium chloride solutions to his animals after operation.

With these views I cannot agree. The loss of water and electrolytes by vomiting in cases of low obstruction is much less rapid than in high obstruction, but there is no doubt that, in any series of dogs with a low obstruction, a definite percentage will die as a result of dehydration and chloride loss. This percentage is increased by allowing the animals water to drink post-operatively.[24] It would appear therefore that, in order to estimate the value of *B. welchii* antitoxin in cases of low obstruction, it is essential that any possible degree of dehydration should be controlled by an adequate replacement of sodium chloride solution. The following series of experiments was carried out with that object in view.

EXPERIMENTS

Eleven dogs in all were used. An identical technique was adopted in each case. The dogs were given gr. ¼ morphine half an hour before operation, which was conducted under ether anæsthesia. The ileum was divided about six to ten inches from the cæcum and the two ends closed and invaginated. A careful asepsis was maintained throughout the operative procedure. After operation the dogs were allowed to drink water as required. Food was not given. Most of the animals vomited the day after operation and the vomiting in small amount continued until the experiment was concluded. It was noted that, after the second or third day, very little water was drunk, although it was always available. All the dogs were given intraperitoneal injections of 1 per cent. sodium chloride solution daily to counteract the dehydration which resulted from the vomiting. At first 250 c.cm. per day was regarded as sufficient but one dog died on the third day after operation from what I thought was dehydration. The dosage was accordingly increased to 750 c.cm., with marked improvement in the animals' condition. Six of the dogs were given at intervals injections of *B. welchii* antitoxin. The concentrated serum—5 units per c.cm.—was used, and each animal received a minimum dosage of 15 units per kg. of body-weight, three times the dose recommended by Williams.[17] The injections were commenced the day after operation and were continued on alternate days. Blood samples were taken at times indicated in the accompanying Table and estimations of the chloride level and non-protein nitrogen (N.P.N.) fractions made. In order to simplify the results and the subsequent comments I have tabulated the order of events as though all the operations were performed on the same day.

Estimations of Non-protein Nitrogen and Chloride in Animals, with Experimental Intestinal Obstruction

Days after operation ..		0	2	4	6	8	11	Day on which animal died.
Dog.	—							
1	N.P.N. ..	31	32	20	27	27	28	12th
	Cl ..	506	487	486	500	473	486	
2	N.P.N. ..	28	30	32	29	30	..	9th
	Cl ..	472	493	496	526	510	..	
3	N.P.N. ..	30	37	20	..	..	..	5th
	Cl ..	504	471	462	..	..	..	
4	N.P.N. ..	27	24	24	22	24	24	12th
	Cl ..	496	522	496	556	532	526	
5	N.P.N. ..	25	36	28	29	27	28	17th
	Cl ..	516	320	431	474	492	484	
6	N.P.N. ..	23	27	21	28	28	26	13th
	Cl ..	522	514	466	556	560	546	
7	N.P.N. ..	24	23	25	23	21	23	15th
	Cl ..	514	507	504	550	511	528	
8	N.P.N. ..	23	32	30	22	26	..	9th
	Cl ..	476	444	408	506	496	..	
9	N.P.N. ..	29	34	22	34	25	27	12th
	Cl ..	514	496	416	525	470	489	
10	N.P.N. ..	27	35	23	31	26	29	15th
	Cl ..	530	431	468	522	546	532	
11	N.P.N. ..	27	33	..	..	..	..	3rd
	Cl ..	452	396	..	..	..	..	

The *B. welchii* antitoxin was given by intramuscular injection to dogs 1–6 in the Table. In considering the results of this series I wish to eliminate dogs 3 and 11. The former died from a widespread peritonitis which probably followed a leakage at one of the suture lines. The latter apparently died from dehydration and sodium chloride loss. In all the remaining animals the autopsy findings were identical, differing only in the degree of distension of the obstructed intestine. The closure of the ends of the intestine was sound and there was no evidence of peritonitis. The portion of intestine immediately proximal to the obstruction was distended to several times its normal size, and the walls were very œdematous and congested. Striking changes were found in the intestinal mucosa. Numerous reddish-coloured areas were evident; the mucosa had been completely shed, and scattered submucous hæmorrhages were sometimes noticeable. These changes were most marked in the two feet of intestine proximal to the obstruction and were seldom evident beyond that distance. The liver was very small and showed marked evidence of fatty degeneration, but this was to be expected as a result of the period of starvation through which the dogs had passed.

It will be seen that the dogs receiving injections of *B. welchii* antitoxin fared no better than the untreated controls. Five dogs receiving the antitoxin lived a total of 63 days, or an average of 12·2, whilst four dogs not receiving the antitoxin lived 51 days, an average of 12·75. The results are fairly even and are not unduly affected by the result of one particular experiment. The chemical estimations on the blood samples are interesting. It appears that the administration of adequate amounts of sodium chloride solution prevents an increase in the concentration of the nitrogenous elements in the blood. Estimations made just before death show no rise in the N.P.N. fraction beyond normal limits. It is probable that the rise in the N.P.N. fraction so frequently noticed in experimental results is dependent upon impairment of renal function owing to dehydration. There is no evidence to associate a rise in the N.P.N. of the blood with the toxæmia of intestinal obstruction. From these experiments it is safe to conclude: (1) that animals with an obstruction in the terminal ileum die in spite of the prevention of dehydration and chloride loss; and (2) that life is not prolonged in these cases by the administration of large doses of *B. welchii* antitoxin.

The results of many other investigations into the problem of the toxæmia of acute intestinal obstruction are no more helpful to the *B. welchii* theory. There is ample evidence that anaerobic, sporulating, gas-forming organisms of the *B. perfringens* group are frequent inhabitants of the terminal ileum and there is no doubt that they proliferate in the lumen of the bowel after obstruction.[17 20 23] The cultural studies of the bacterial flora of obstructed loops carried out by McIver and his associates [20] deserve careful consideration. They found that there was no noteworthy increase of any organisms of the aerobic group but that the numbers of the *B. welchii* group were always increased and in no case was there any doubt that *B. welchii* was the predominant organism. They drew attention to the fact that different strains of *B. welchii* show marked variations in their ability to produce toxin, and proceeded to determine the variations in the organisms isolated from obstructed loops. Fourteen strains were used and of these eight were entirely devoid of demonstrable toxicity. Only two strains developed a toxin which compared favourably with that elaborated by a strong toxin-producing stock strain. The hæmolytic power of the *B. welchii* toxin is well known, and animals dying as a result of a lethal dose of toxin show at autopsy evidence of a definite hæmolysis with bloody fluid in the chest and abdominal cavities. But Owings and McIntosh [19] bring out in their paper the evidence that the hæmolysis that follows the intravenous injection of a lethal dose of loop toxin is very much less than that resulting from an injection of *B. welchii* toxin. They show that immunity to the *B. welchii* toxin affords no protection against an injection of the loop toxin, and point out that animals may be successfully immunised against *B. welchii* toxin. These findings have been confirmed by Thurston.[23] Dragstedt [25] was unable to demonstrate the development of any immunity in animals subjected to injections of sublethal doses of the loop toxin. Furthermore, the substance is not destroyed by boiling[26]; it is held up by a Berkefeld filter [27] and it is precipitated by five volumes of alcohol.[28] The striking similarity between the pharmacological actions of the toxic substance and those of the proteoses has been mentioned by Whipple [29] and Chittenden.[30] Thus, while there is still considerable doubt as to the exact nature of the toxic substance present in obstructed loops of intestine, the bulk of evidence is not in favour of its being a bacterial exotoxin.

CONCLUSION

B. welchii is the predominant organism present in obstructed or strangulated loops of intestine. The suggestion that the absorption from the obstructed bowel of the exotoxin of *B. welchii* is responsible for the toxæmia of acute intestinal obstruction is not borne out by later experimental work. It is important to observe that some of the earlier work which appeared to support the *B. welchii* theory was the result of experimental obstruction of a type in which toxæmia is not a lethal factor. There has now accumulated a sufficient amount of evidence from types of cases in which death is usually due to a toxæmia to suggest that the *B. welchii* toxin does not play an important rôle in acute intestinal obstruction. It is only fair to state that, on the clinical side, Williams [17] and Bower and Clark [21] have felt that improvement followed the use of *B. welchii* antitoxin in the treatment of their cases of acute obstruction. But before this opinion can be established it will be necessary to bring forward a series of carefully controlled cases with a type of intestinal obstruction in which death results from toxæmia. The mere presence of *B. welchii* in large numbers in the obstructed segment of intestine by no means proves that it is a factor of importance in producing the symptoms of the disease. Cultures of the organism from cases of acute obstruction show a large number of avirulent strains, a feature which appears to be characteristic of the strains of *B. welchii* isolated from the fæces or from wounds of the perineum and adjacent localities, where the organisms produce little or no toxin and cause no clinical symptoms of infection. But the part played by *B. welchii* in the pathology of acute intestinal obstruction cannot be summarily dismissed. Its proteolytic power is probably of great importance in the production of the toxin of acute obstruction if the view is accepted that the toxin is probably a proteose and its gas-producing power is partly responsible for the marked distension of the obstructed segment which precedes any absorption of the toxin. In this way it is probable that *B. welchii* plays an important part in the development of the toxæmia of acute obstruction. But the experimental evidence does not support the view that the exotoxin of *B. welchii* plays any part in the toxæmia of acute obstruction, and the use of

the antitoxin has not proved of any value in the treatment of those types of acute obstruction in which a toxæmia is believed to exist.

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THE TREATMENT OF TETANY

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The so-called carpo-pedal spasms characteristic of tetany consist in flexion of the metacarpo-phalangeal joints with extension of the other phalangeal joints and opposition of the thumb. The resulting position is called, for obvious reasons, "main obstétricale." Similar contractions occur in the foot and there is often simultaneous spasm of the facial muscles and chest. Severe attacks may be complicated by epileptiform cramps.

Tetany may, however, be present when no carpo-pedal spasms are seen. The existence of this "latent tetany" is indicated by—

1. *Chvostek's sign.*—Percussion of the cheek just in front of the external auditory meatus causes contraction of the facial muscles.

2. *Trousseau's sign.*—A typical carpal spasm appears when the upper arm is compressed for a minute or two.

3. *Erb's sign.*—Electrical stimulation of the nerves of the arm reveals an increased and abnormal irritability of the peripheral nervous system.

4. *Schlesinger's sign.*—A typical pedal spasm is produced by flexing the hip-joint with the knee extended, the patient being recumbent.

5. All patients with tetany have a tendency to develop cataract and trophic disturbances of the nails and teeth.

Manifest and latent tetany have one general cause—hypocalcæmia. When the calcium content of the blood-serum falls below 7 mg. per 100 c.cm. symptoms of tetany usually appear. Hypocalcæmia can be produced by various causes but this paper deals with two kinds only—namely, lesions of the parathyroid (parathyroprive tetany); and idiopathic—apparently causeless—tetany in which the function of the parathyroids is supposed to be diminished.

The prognosis of tetany has improved during the last decade, the treatment consisting in administration of calcium. Only a small part of any calcium taken by the mouth is absorbed from the intestine, and intravenous injections, though they can now be given without risk and almost always cut short an acute attack, have only a temporary beneficial effect. Vitamin D, when given with the calcium, improves absorption from the intestine. Subcutaneous injection of the active principle of the parathyroid, discovered by Collip in 1927 and marketed as Parathormone, causes a considerable increase in the blood calcium and will almost always counteract tetany. Only in very severe chronic cases do these three methods completely fail. Unfortunately treatment with parathormone is very expensive and its influence on hypocalcæmia gradually diminishes.

SURGICAL TREATMENT

Transplantation of parathyroid gland is usually ineffective; the transplant rarely survives, though temporary favourable results have been obtained, and the attacks of tetany generally recur after a few weeks or months. Gold [1] has recently reported one case in which parathyroid transplantation was successful.

Case 1.—A woman was operated on for goitre in 1902. The operation was followed by a short period of tetanic symptoms, but these disappeared spontaneously and did not recur during subsequent pregnancies. Severe tetany, however, developed 13 years after the original operation. Transplants were made in 1920, 1921, and 1924, on each occasion being followed by temporary improvement. In 1930 the symptoms were serious, despite treatment by parathormone and calcium. In 1931 the attacks were accompanied by epileptiform convulsions, delirium, and dementia. Two more transplant operations were undertaken in March and April, 1931; the epileptiform cramps disappeared after the first, and the other symptoms after the second, and since then the patient has been able to go back to full work.

TABLE I

Serum calcium and inorganic phosphate in a case of parathyroprive tetany improved by transplantation of parathyroids (Gold).

	Serum Ca mg. per 100 c.cm.	Inorg. phosph. mg. per 100 c.cm.
Before transplantation	5·40	7·10
3 days after „	6·80	5·03
7 „ „	8·80	4·60
1 month „	12·50	7·70
7 months „	11·80	5·26
1 year „	5·90	4·95
1½ years „	8·20	5·70

The calcium content of the serum was less than 6 mg. per 100 c.cm. before the operation, and the inorganic phosphorus was very high: 7 mg. per 100 c.cm. instead of the normal 3·5 mg. (Table I.). After the 1931 operation the calcium became normal, and for a short time there was a slight but definite hypercalcæmia. The phosphorus reading, however, is still too high, indicating an incomplete function of the transplanted parathyroid. It is usual for the inorganic phosphorus to be high in idiopathic tetany and in tetany due to inadequate parathyroid function; there are, however, forms of tetany where both the

calcium and the inorganic phosphorus are low—e.g., when fatty diarrhœa causes tetany.

In another case under my observation the transplantation of parathyroid saved the life of a patient with very severe tetany.

CASE 2.—A woman of 35 was operated on for goitre in 1915 and again for recurrence in 1924. Four days after the second operation typical tetany developed and was unaffected by very large doses of calcium lactate and parathyroid by the mouth. The attacks became more frequent and were soon accompanied by epileptiform convulsions. They were with difficulty controlled by the administration of 6 g. of chloral hydrate, and several injections of Pantopon daily. Dementia, complicated by attacks of delirium, developed, and this condition lasted for three months. At the end of that time Prof. Lanz transplanted two human parathyroids into the abdominal muscles. This operation immediately stopped the attacks, and the patient was able to go home after a period of convalescence.

Five years later she was examined again. She then felt completely well and took only calcium lactate and thyroid by the mouth. She had a severe attack of tetany in 1933 and came for examination a week later. Chvostek and Trousseau signs could not be evoked, but the calcium content of the serum was found to be 6·2 mg. per 100 c.cm. and the inorganic phosphorus 4·3 mg. The patient had previously been taking only one teaspoonful of calcium lactate; this dose was increased to two teaspoonfuls three times daily, together with two tablets of vitamin D. The symptoms disappeared completely. In September, 1933, the blood calcium was 8·07 mg. and the inorganic phosphorus 3·75.

In these two cases the benefits conferred by the transplantation of the parathyroids was lasting. Possibly in both one parathyroid gland was present but damaged, and was able to recover during the time when the transplant was being absorbed. Even so it would be remarkable that the attack should have lasted for more than three months and have become gradually worse in the presence of a damaged but recovering gland. It seems possible that the transplant may not have been absorbed, and it is at any rate certain that the operation saved the patient's life.

PARATHORMONE TREATMENT

Completely satisfactory results can also be obtained by continuous treatment with parathormone, as the following case shows.

CASE 3.—Another woman, aged 76, had typical carpopedal spasms in March, 1929, for the first time in her life. In May she had an attack of cardiac asthma and five days later a second attack of tetany. Two days later she suffered a third attack of tetany, and a week after that another attack of cardiac asthma. She was given calcium lactate, digitalis, and ouabaine by the mouth and improved somewhat, but during the succeeding summer she lost all her nails. In January, 1930, she developed cataract in both eyes and suffered from continual facial cramp when talking. Parathyroid tablets (by mouth) were started in June. In January, 1931, her condition was worse. She suffered from anorexia, stiffness in the fingers, cramps when talking, diminished eyesight, and crumbling nails. On May 6th, 1931, her blood calcium was only 4·9 mg. per 100 c.cm., although the inorganic phosphorus had not increased above 4·03 mg. (Table II.). Since then she has had 1 c.cm. of parathormone subcutaneously each day and her condition has improved from the first injection; the eyesight is better and the cramps have disappeared. After three weeks of parathormone treatment the blood calcium and phosphorus were normal and the dose was reduced to 1 c.cm. on alternate days. On June 25th she showed a slight hypercalcæmia and the dose was thereafter given every four days. After some trials a dose on alternate days was found to keep her blood calcium at the best level and this treatment has been continued up to the present. The patient feels well; she has no attacks of tetany and no heart trouble and her nails are normal. After a complicated cataract operation in 1933 she had a severe broncho-pneumonia from which she recovered.

TABLE II

Case of idiopathic tetany successfully treated with parathormone injections for 2¼ years

1931.	Serum Ca mg. per 100 c.cm.	Inorg. phosph. mg. per 100 c.cm.	Parathormone.
April 30	5·02	4·02	Before treatment.
May 4	4·98	—	1 c.cm. every day.
,, 27	10·14	3·28	1 c.cm. every 2 days.
June 25	13·32	4·70	1 c.cm. every 4 days.
Oct. 9	7·93	—	,, ,, ,,
,, 17	8·83	—	1 c.cm. every 2 days.
Dec. 22	9·49	—	,, ,, ,,
1932.			
Oct. 23	9·40	—	,, ,, ,,
1933.			
Dec. 11	9·51	—	,, ,, ,,

TREATMENT BY A.T. 10

Some patients, however, cannot be kept in good health by any combination of surgical or medical methods. A new preparation has been discovered recently and has proved far more active than any of those previously used. Excessive doses of irradiated ergosterol may cause disagreeable or even dangerous symptoms which are usually accompanied by hypercalcæmia. Holtz,[2] working with Windaus in Göttingen, has made a study of the different fractions of irradiated ergosterol and has succeeded in isolating one portion which does not contain vitamin D but which has a specific influence on the calcium content of the serum. It is an oil-soluble fraction, standardised on mice, and known as A.T. 10. When taken by the mouth it causes hypercalcæmia in animals and men; the effect is less rapid than that produced by subcutaneous injection of parathormone but is more lasting. During the first few days after administration of A.T. 10 there is no considerable increase of blood calcium, but the dose should not therefore be increased, because if it is there will be accumulation and dangerous hypercalcæmia.

Holtz, in his investigations at the Charité Hospital in Berlin, has worked out the following treatment, which has proved reliable. In severe cases of tetany 5 to 10 c.cm. of A.T. 10 is given daily for three days. After this the dose must be considerably restricted, even if there is no increase in the blood calcium, lest hypercalcæmia and calcification of organs, especially the kidneys, results. Prolonged administration in correct dosage, however, is not dangerous. Holtz gave A.T. 10 to parathyroidectomised dogs for over a year and could find no symptoms of damage on autopsy.

I have tried A.T. 10 in three cases of tetany, one idiopathic and two parathyroprive. The blood calcium did not exceed 6 mg. per 100 c.cm. in any of them. I therefore began by giving 10 c.cm. of A.T. 10 on the first day and 5 c.cm. on the second and third days. Thereafter 1 to 2 c.cm. was given daily for a short time. In all the patients the calcium content of the serum increased considerably after three to five days and the symptoms of tetany disappeared. After the first ten days a dose of 1 to 2 c.cm. three times a week was usually sufficient to keep the calcium content normal. All other therapeutic measures could be stopped a day or two after the beginning of the A.T. 10 treatment.

This simple oral method of handling tetany is a great improvement on previous techniques; it can only be applied, however, in cases where the calcium content of the serum can be watched, as otherwise there is a risk of accumulation. For this reason the manufacturing firms only put A.T. 10 at the disposal of clinicians working in hospitals where calcium analyses are done regularly.

CASE RECORDS

CASE 4.—A woman, aged 42, had had thyroidectomy performed in 1924 and again in 1932. After the second operation, cramps in the hands, feet, and head had appeared, and a month later had become worse, being accompanied by epileptiform seizures. The latter disappeared under parathormone and calcium treatment and the tetany was relieved, but she still suffered from rigidity of the hands and feet and speech difficulties. Chvostek, Trousseau, and Schlesinger signs remained positive. The calcium content of the serum varied between 4 and 6 mg.

TABLE III

Tetany after thyroidectomy. Parathormone treatment insufficient: immediate result of administration of A.T. 10

1933.	Serum Ca mg. per 100 c.cm.	Inorg. phosph. mg. per 100 c.cm.	Treatment.
June 30	4·80	6·61	
Aug. 5	6·20	—	
„ 14	—	—	4 c.cm. parathormone (80 units) subcutaneously.
„ 17	6·65	5·48	
„ 19	6·44	—	10 c.cm. calcium. Sandos intravenously twice daily.
„ 22	5·86	—	
„ 22	—	—	3 drops vitamin D, t.d.s.
„ 25	5·50	—	Aug. 14th, 22nd, and Sept. 19th: transplantation of two parathyroids.
Sept. 5	6·20	6·05	
„ 19	—	—	
„ 25	4·80	6·04	
„ 27	—	—	10 c.cm. A.T. 10
„ 28	—	—	5 „ „
„ 29	—	—	5 „ „
„ 30	8·80	6·77	1 „ „
Oct. 1	—	—	1 „ „
„ 2	8·75	3·65	No „
„ 3	—	—	1 c.cm. „
„ 4	—	—	1 „ „
„ 5	8·94	4·37	No „
„ 6	—	—	1 c.cm. „
„ 7	—	—	No „
„ 8	—	—	„ „
„ 9	8·99	3·97	1 c.cm. A.T. 10*
„ 16	10·95	3·86	
„ 17	—	—	No A.T. 10†
„ 23	8·05	4·44	„ „
„ 26	8·25	4·63	„ „
„ 30	8·00	4·62	„ „
Nov. 2	7·60	4·44	„ „
„ 6	7·30	4·63	„ „
„ 7	Tetany		2 c.cm. A.T. 10
„ 8	—	—	2 „ „
„ 9	8·00	4·67	2 „ „‡
„ 13	8·65	4·27	2 „ „
„ 16	9·80	4·14	2 „ „

All other treatment stopped.

* 1 c.cm. A.T. 10 every second day from Oct. 9th to 17th.
† None from Oct. 17th to Nov. 7th.
‡ 2 c.cm. A.T. 10 every second day from Nov. 9th to 18th.

per 100 c.cm (Table III.). The inorganic phosphorus of the blood was considerably increased: 5·5 to 6·2 mg. per 100 c.cm. The teeth showed caries and white patches, but the nails were normal and there were no symptoms of cataract. To attain this state of affairs the patient had to receive 80 units of parathormone subcutaneously and two 10 c.cm. doses of Calcium Sandos intravenously, with three drops of vitamin D thrice, every day. Every attempt to reduce this intensive treatment was followed by severe attacks of tetany. Three transplantations of human parathyroid were made without result. On Sept. 25th, 1932, the calcium content of the blood was 4·8 mg. and the inorganic phosphorus 6·04.

A.T. 10 treatment was started on Sept. 27th, 10 c.cm. being given on the first day and 5 c.cm. on the second and third days. On the fourth day the calcium content of the serum was 8·8 mg., but the phosphorus was not increased. All other methods of treatment were then stopped and the patient for the next ten days was given 1 c.cm. of A.T. 10 for two days, missing the third day. The calcium and phosphorus values then read 8·99 and 3·97 mg. per cent. respectively. From Oct. 9th to 17th 1 c.cm. was given on alternate days and the calcium and phosphorus readings were 10·95 and 3·86 mg. per 100 c.cm.

The A.T. 10 treatment was then stopped for three weeks until Nov. 7th. The blood calcium diminished to 7·3 mg. and the phosphorus went to up 4·63. On Nov. 7th the patient had a definite attack of tetany. She was therefore given A.T. 10 in daily doses of 2 c.cm. for three days and then 2 c.cm. every other day. After a week the calcium had gone up to 8·65 mg. and the phosphorus had gone down to 4·27. After ten days, normal values of both were found.

In this very severe case of parathyroprive tetany, where even large subcutaneous doses of parathormone and intravenous calcium failed to obtain a satisfactory result, A.T. 10 worked like magic. The second case shows a similarly favourable result.

CASE 5.—A woman, aged 48, was operated on for goitre in 1920 and in 1931. A month after the second operation she complained of pricking in the fingers, vertigo, headache, and fatigue, and the diagnosis of parathyroprive tetany was made in Germany in November, 1931. She received injections of a German parathyroid preparation for five months without benefit, and in April, 1932, severe cramps with general rigidity and cyanosis developed. In July she showed all the symptoms of latent tetany. She had severe hypocalcæmia and an increase of inorganic phosphates. At first she would not take parathormone injections because she thought she got sufficient relief from taking calcium and vitamin D by the mouth. In December, however, she suffered so much from general weakness and fatigue that she began taking 20 units of parathormone on alternate days, continuing to take calcium and vitamin D. On this treatment her condition was satisfactory but she always showed symptoms of latent tetany; she was always tired and her blood was hypocalcæmic (6 to 7 mg. per 100 c.cm.). Under parathormone treatment, however, the inorganic phosphorus became normal (Table IV.).

A.T. 10 treatment was started on Oct. 17th, 1933: 5 c.cm. on the first day, 10 c.cm. on the second day, 5 c.cm. on the third day, and 2 c.cm. on the fourth day. On the fifth day the calcium in the serum had increased from 6 mg. per 100 c.cm. to 8·4 mg. In the six succeeding days she was given 1 c.cm. of A.T. 10 daily and thereafter

TABLE IV

Tetany after thyroidectomy, latent tetany during parathormone treatment. On oral administration of A.T. 10 the calcium of the serum increased to normal values

1932.	Serum Ca mg. per 100 c.cm.	Inorg. phosph. mg. per 100 c.cm.	Treatment.
July 19	6·72	6·30	
„ 26	7·10	6·72	
Aug. 5	8·80	—	Calcium and vitamin D by mouth.
Oct. 26	5·90	4·96	
Nov. 16	6·90	—	
Dec. 7	7·00	5·47	
1933.			
March 17	5·60	—	
April 4	6·60	—	1 teaspoonful of calc. lact., and
July 7	5·70	4·41	15 drops vitamin D, t.d.s.
Sept. 28	7·25	4·73	Every two days: para-
Oct. 12	7·20	3·59	thormone 1 c.cm. (20 units).
„ 16	6·00	3·78	
„ 17	—	—	5 c.cm. A.T. 10.
„ 18	6·10	—	10 „ „
„ 19	—	—	5 „ „
„ 20	—	—	2 „ „
„ 21	8·40	—	1 „ „*
„ 26	9·20	—	1 „ „†
Nov. 8	8·70	4·34	1 „ „
„ 24	9·10	—	1 „ „

* 1 c.cm. A.T. 10 daily from Oct. 21st to 26th.
† 1 c.cm. A.T. 10 every second day from Oct. 26th to Nov. 24th.

1 c.cm. on alternate days. All other treatment was stopped when the A.T. 10 treatment was started. The calcium remained about 9 mg. per 100 c.cm., and the general condition improved rapidly. The patient felt much better and was able to resume her normal activities.

CASE 6.—A man, aged 48, had a long-standing idiopathic tetany. At the age of 30 he had developed double cataract which had been operated on four years afterwards. Apart from this he had felt quite healthy until 1927, when he

had complained of fatigue and cramps in the fingers, especially when overworked. In January, 1933, he had an attack of acute tetany in the street, and after that his fatigue increased so much that he could not continue working; his nails crumbled away and attacks of tetany appeared from time to time. In January, 1930, he showed severe hypocalcæmia and high phosphate content (6 to 6·5 and 5 to 6·6 mg. per 100 c.cm. respectively). Two parathyroids were transplanted with no effect at all. Parathormone injections were given between July 7th and 31st, and the serum calcium rose to 10 mg., the serum phosphate dropping to 3·36. As soon as the injections were stopped the calcium content decreased again to 6 mg. The man attended the out-patient department regularly; although he had severe hypocalcæmia all the time his only complaints were fatigue and chilliness. This is in accordance with the general experience that symptoms of chronic tetany become less marked after a lapse of time. Nevertheless, the patient was a chronic invalid unable to do regular work.

TABLE V

Latent idiopathic tetany. No influence of transplantation of two parathyroids. Transient result of parathormone injections. On oral administration of A.T. 10 the calcium of the serum increased to normal values

1930.	Serum Ca mg. per 100 c.cm.	Inorg. phosph. mg. per 100 c.cm.	Remark.
June 17	6·08	5·04	Low calcium diet.
„ 21	6·48	6·00	Mixed diet.
July 3	6·21	6·60	—
„ 4	..		Transplantation of parathyroids.
„ 7	6·60	5·28	—
„ 16	7·77	5·76	—
„ 21	7·52	5·52	Low calcium diet.
„ 24	6·45	—	Low calcium diet + 5 g. calc. lact.
„ 27	7·69	5·68	50 U. parathormone + 5 g. calc. lact.
„ 28	8·35	4·80	60 U. parathormone + 5 g. calc. lact.
„ 29	10·00	3·60	70 U. parathormone + 5 g. calc. lact.
„ 30	9·91	3·36	40 U. parathormone + 5 g. calc. lact.
Nov. 24	5·15	6·06	
1931.			
Dec. 22	5·00	—	Discharged from hospital.
1932.			
July 11	5·21	6·46	
1933.			
Jan. 31	5·80	6·36	Before treatment.
Oct. 14	5·42	6·40	
„ 16	—	—	10 c.cm. A.T. 10.
„ 17	—	—	5 „ „
„ 18	4·80	7·10	5 „ „
„ 19	—	—	2 „ „
„ 20	—	—	2 „ „
„ 21	7·07	6·77	1 „ „
„ 23	—	—	1 „ „
„ 25	9·05	4·63	1 „ „
„ 27	—	—	1 „ „
„ 28	9·34	5·50	—
„ 30	—	—	1 c.cm. A.T. 10
Nov. 2	—	—	1 „ „
„ 6	10·10	4·45	0·5 „ „
„ 10	—	—	0·5 „ „
„ 14	9·13	3·97	0·5 „ „
„ 18	—	—	0·5 „ „
„ 22	—	—	1 „ „
„ 27	8·53	4·66	1 „ „
Dec. 1	—	—	1 „ „
„ 5	9·80	4·95	1 „ „

A.T. 10 treatment was started on Nov. 16th, 1933: 10 c.cm. on the first day and 5 c.cm. on the second and third days (Table V.). The calcium and phosphorus readings on the third day were 4·8 and 7·1 mg. per 100 c.cm. respectively, but the dose was nevertheless decreased and 2 c.cm. given for the next two days; then the calcium content was found to have risen to 7·01 mg. For a week 1 c.cm. was given every other day and the calcium and phosphorus readings were then 9·34 and 5·4 mg. respectively. The calcium remained normal and the inorganic phosphate went down to 4·5 mg. under doses of 0·5 and 1 c.cm. of A.T. 10 every few days. The patient became another man under this treatment. He had much more energy and no longer suffered from chilliness. His skin, previously extremely dry, became normal; in fact he only discovered how much he had suffered from his chronic hypocalcæmia when his blood calcium was restored to normal.

SUMMARY

(1) The transplantation of parathyroids for the treatment of tetany does not have a lasting effect although in exceptional cases it may save life. (2) For milder cases the administration of calcium and vitamin D by the mouth is often enough. (3) In most of the more severe cases improvement can be obtained by intravenous injections of calcium and subcutaneous injections of parathormone. (4) A great improvement in the methods of treatment available is represented by oral administration of A.T. 10, a by-product of the irradiation of ergosterol, small doses of which will restore the blood calcium to normal level in the severest cases of tetany, both parathyroprive and idiopathic. (5) The cumulative action of A.T. 10 must not be overlooked; after initial doses of 5 to 10 c.cm. for three days the dose must always be reduced to 1 or 2 c.cm. daily for ten or fourteen days, after which 1 to 2 c.cm. three times a week is sufficient, even in the severest cases.

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THE MECHANISM OF HOMOLOGOUS TUMOUR IMMUNITY

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IN a paper[1] on the nature of immunity to transplanted tumours, published by one of us (T. L.) in 1927, it was stated that in the case of immunity against a homologous tumour—for example, in a rat immune to Jensen's rat sarcoma (J.R.S.)—anti-cancer bodies were present in the immune animal's serum. This conclusion, vigorously opposed in certain quarters, was inferred from a number of experimental observations, but it could not at that time be directly demonstrated on tissue cultures of the tumour cells concerned. This difficulty has been surmounted and the presence of antimalignant-cell bodies can now be shown directly and conclusively by applying the immune rat's serum to cultures of J.R.S. cells in vitro under appropriate conditions.

The probable reason why this fundamental observation eluded previous investigators is that its vivid demonstration requires the coincidence of three separate conditions or factors, each of which, although contrary to expectation, is yet essential.

In order that the immune serum shall invariably kill the J.R.S. cells to which it is applied it is necessary that:—

1. The serum be drawn soon, preferably on the third day, after the last immunising inoculation. The titre of antibodies rises rapidly for the first 48 hours, thus

[1] THE LANCET, 1927, i., 116.

attaining its maximum unusually early. From 48 to 96 hours it is at its highest, and it falls again equally rapidly, so that by the sixth or seventh day it may be so low as to be difficult to demonstrate.

2. The serum should be applied to young (24 hours old) actively growing J.R.S. cultures. With older cultures the reaction is much less striking.

3. The serum must be applied directly after it has been prepared, since the antibodies are exceedingly labile and may become ineffective if kept at laboratory temperature for an hour or two.

The characteristic effect of a strong serum is that it kills the J.R.S. cells within 10–30 minutes. The cells swell up, their nuclei become sharply defined and shrunken, and the fatty and protoplasmic granules agglutinate. If stained after 6–8 hours the

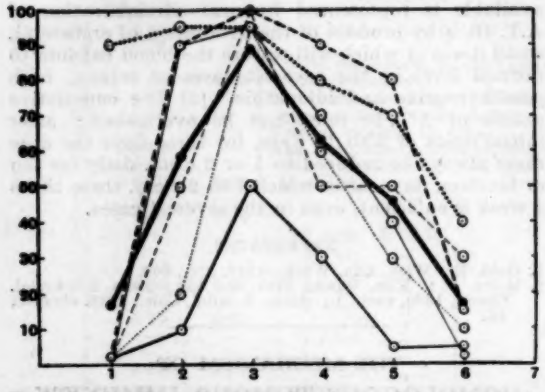

Chart showing the anti-cancer-cell potency of the sera of six rats immunised against a homologous tumour. The abscissæ show the percentage of migrating J.R.S. cells killed by the respective sera, while the ordinates represent the period at which the sera were drawn, in days, after the last injection of antigen (J.R.S.). The darkest black line is the average of all the observations; the other lines represent daily the variations in the titre of the serum of each of the six rats. All the cultures used were of comparable vigour each containing several hundreds of actively migrating sarcoma cells.

nuclei are found to be pyknotic, while if 24 hours are allowed to elapse before staining, complete chromatolysis is seen to have taken place. Cultures of normal tissue cells are entirely undamaged by these powerful anti-cancer sera.

When the above precautions are taken the results are characteristic and consistent in 100 per cent. of the experiments; the sera of a rat hyper-immunised against J.R.S. kill the actively migrating J.R.S. cells, whereas control sera from normal rats similarly drawn and applied have no damaging effect at all on the J.R.S. cultures.

A full account of the methods, protocols, and evident extensions, of the experiments here referred to, will be published in the near future. It may suffice in this preliminary note to illustrate in graphic form one typical experiment showing the rise and fall of the titre of the anti-cancer bodies and their effects in a series of six rats.

We draw the following conclusions: (1) That the presence of an effective titre of anti-cancer bodies is demonstrable in the serum of an animal immunised against a homologous tumour. (2) That the existence of these antibodies provides an adequate explanation of the mechanism of homologous tumour immunity.

The experiments referred to above have been performed with the help of grants from the British Empire Cancer Campaign, which have made it possible for each of the three authors to devote his whole time to cancer research.

THE INCIDENCE OF ADENOMA OF THE PITUITARY BODY IN SOME TYPES OF NEW GROWTH

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The incidence of tumours in endocrine glands has recently become a matter of importance, since it is now clear that the presence of these tumours is associated in many instances with the effects of hyper-secretion of their respective glands. In a series of pituitary bodies obtained from routine post-mortem examinations at Guy's Hospital in the past 18 months, not only was the incidence of tumours in the pituitary body one of the principal objects of investigation but their presence in relation to clinical signs or symptoms was also noted.

Unfortunately, it was not found practicable to examine the pituitary body in every case, and the first 200 glands were collected from 450 consecutive cases. This group cannot, therefore, be called a true random sample, but on the other hand no deliberate choice was exercised. The selection was determined by the necessity of opening the skull—as, for example, in all cases of accident and sudden death (33); in all cases of probable cerebral involvement (40); and in many instances where a brain was required for anatomical purposes (127). In this way it was found possible to obtain a fairly representative number of both sexes (132 males, 68 females) and all ages, the average number for each decade between the ages of 10 and 70 being 30.

On removal from the sella turcica the pituitaries were fixed in 10 per cent. formol saline and cut in the horizontal plane—i.e., through the equator if the stalk were to represent the north pole. The sections were stained both with hæmatoxylin and eosin in the usual way and with a slight modification of Mallory's connective tissue stain. The use of some stain such as the latter is essential if the cells of the anterior lobe are to be classified correctly as chromophobe, acidophil, or basophil.[1]

In an investigation of this nature where all degrees of deviation from the normal appearance of the pituitary may be encountered, it is imperative that the term "adenoma" should be clearly defined. "Adenoma" is used here to describe a grouping together of one of the three types of cells found in the anterior lobe. An arbitrary limit for the diameter of an adenoma was fixed at 0·8 mm., the smallest found, but the majority of these tumours can be seen easily in the stained sections by the naked eye. The nodule of growth may be solid or partly cystic and may or may not have a fibrous boundary, but is easily distinguishable from the neighbouring cells by alterations in the arrangement, size, and shape of the cells. The normal acinose plan is lost, the stroma is often scanty, and the cells are smaller than normal. The not infrequent hyperplasia of cells confined to one acinus only has not been regarded as adenoma, and doubtful "border line" tumours have been rejected.

An examination of a few sections only from the plane through which the pituitary had been cut was made at first and revealed several points of interest. For example, in the first 200 pituitaries collected as described above, an adenoma was found in 18—i.e., the incidence of pituitary adenomata is probably at least 1 in 10. This is in agreement with the findings of other investigators.[2,3] It was also

noticed that most of these adenomata were present in subjects of more than 45 years of age who had, in addition, a benign or malignant new growth in some other part of the body.

Attention was thereupon directed to testing the correctness of this latter observation: 125 pituitaries were subjected to serial sectioning, 75 from cases of proved new growth occurring elsewhere in the body, and 50 from "control" cases. The latter, the "controls," were subjects of 45 years of age or more in whom routine post-mortem examination (conducted with varying thoroughness, particularly in regard to the thyroid and sex glands) revealed to the naked eye no obvious new growth. Serial sections were cut at a thickness of 7μ and from six to twelve sections were placed on each slide, about forty slides being required for a normal-sized pituitary. Every fourth slide was stained and examined. Five of the "control" cases had an adenoma of the pituitary—an incidence of 1 in 10—and the sex, age, and post-mortem diagnosis in these cases are briefly as follows:—

1. Male, 54 years. Gastro-jejunostomy four months before dying of acute pancreatitis.
2. Male, 60 years. Gastro-jejunostomy six years before dying of acute duodenal obstruction.
3. Male, 54 years. Inguinal hernia for 20 years before it strangulated. Had a generalised hyperplasia of lymphoid tissue and a persisting thymus.
4. Male, 55 years. Died of cerebral hæmorrhage.
5. Male, 62 years. Died on admission. Thrombosis of coronary arteries of heart.

In four other cases of cerebral hæmorrhage and four other cases of sudden heart failure no adenomata were found in the pituitary.

—	Pituitaries examined.	Pituitaries with adenoma.	Incidence of adenoma of pituitary.
(A) Controls	50	5	1 in 10
(B) Adenoma of prostate ..	10	8	8 in 10
(C) Carcinoma—			
Epithelioma ..	10	0	—
Glandular ..	52	23	4·4 in 10
(*a*) Pancreas ..	8	6	7 in 10
(*b*) Rectum ..	10	6	6 in 10
(*c*) Bronchus ..	7	4	6 in 10
(*d*) Stomach ..	10	3	3 in 10
(*e*) Colon ..	6	2	3 in 10
(*f*) Prostate ..	5	1	—
(*g*) Breast ..	2	0	—
(*h*) Uterus ..	2	0	—
(*i*) Ovary ..	1	1	—
(*j*) Suprarenal ..	1	0	—
(D) Sarcoma	6	2	3 in 10
(E) Lymphadenoma ..	2	1	—
Total	130	39	—

INCIDENCE OF ADENOMATA

The most striking feature of the Table is the comparatively high incidence of pituitary adenomata in cases of adenoma of the prostate and carcinomata of the pancreas, rectum, and bronchus. In the "control" cases the incidence of pituitary adenomata is only 1 in 10, so that even if the figures are too small statistically to allow definite conclusions to be drawn, they nevertheless suggest that some association exists between pituitary adenomata and certain kinds of new growth. What form this association takes is not at all clear, but four possibilities may be suggested.

First, it is well recognised that the pituitary plays some part in the growth of the body considered as a whole. Evans and others have produced gigantism in animals by injections of extract of anterior lobe [4]; and the frequent association of acidophil adenoma with acromegaly also points to a hypersecretion of the anterior lobe as the probable cause of increased stature. There is, however, no reason to believe that the pituitary can also exert this influence locally to form a new growth, though it may perhaps affect the rate of growth in one particular part, as for example in a neoplasm.

There is a striking difference in the histological appearance of a pituitary taken from a case where there is a slowly growing tumour—e.g., an epithelioma—and one taken from a case where there is a rapidly growing tumour—e.g., a sarcoma. In the epitheliomata the anterior lobe appears to be almost inactive. There are abnormally few cells in each acinus and the stroma is swollen with a "colloid"-looking substance. In the sarcomata, on the other hand, the appearance of the gland suggests a state of great activity. The acini are packed with the increased number of cells and the stroma is inconspicuous. In the cases of glandular carcinomata no correlation has yet been found between the degree of malignancy (as measured by the tendency to infiltrate and metastasise) and the presence of pituitary adenomata or cellular hyperplasia. But if the rate of growth of an active tumour in the body is increased when a pituitary adenoma is present, it would be difficult to explain the frequent association of pituitary adenomata with the less active forms of new growth, such as adenoma of the prostate.

The second suggestion to be put forward may perhaps overcome this difficulty. It is possible that the formation of a tumour in the pituitary, such as an adenoma, is only one indication of a constitutional tendency to tumour-formation in all the glands. For, as the Table shows, the incidence of pituitary adenoma is high in cases of new growth in other glands (adenoma of the prostate and glandular carcinomata), while in cases of epitheliomata not one pituitary adenoma was found. Excellent examples of cases showing widespread tendency to tumour-formation of glands have been described by Cushing and Davidoff [5] and by Simpson.[6]

Thirdly, as very little is known of the effect on the body of a chromophobe cell adenoma in the pituitary, it is possible that an undetected syndrome is associated with the pituitary adenoma present in those types of new growth which have a high incidence of pituitary adenomata as well as in the five "control" cases.

The last of the four possibilities—and the least likely—is that the presence of pituitary adenoma is accidental and unrelated to the presence of other new growths or to a syndrome common to them and to the control cases.

Carcinoma of the pancreas.—The fact that a pituitary adenoma was found in most cases of carcinoma of the pancreas is one more example of the close relationship between the pituitary and the pancreas. Among the other examples are, briefly, the changes which occur in one organ when the other is removed experimentally [7 8]; the mutual antagonism of posterior pituitary extract and insulin [9]; the incidence of diabetes mellitus (12 per cent.) and glycosuria (25 per cent.) in acromegaly [10]; the finding of glycosuria also in cases of basophil cell adenoma of the pituitary.[11]

Adenoma of the prostate gland.—The association of chromophobe adenomata of the pituitary with adenomata of the prostate gland may also be explained on a physiological basis. One of the secretions of the anterior lobe of the pituitary is known to have a gonadotropic effect [12]; and in hypophysectomised rats, feeding with the "anterior pituitary-like

substance" (Collip [13]) led to great hypertrophy of the accessory sexual organs. It should be noted, however, that most of the pituitaries in cases of carcinoma of the prostate appear to be normal histologically. Of the 10 cases of adenoma of the prostate shown in the Table, three were also cases of Paget's disease of bone, and in two of these there was a chromophobe adenoma in the pituitary.

Carcinoma of rectum.—Little can be said as to possible reasons for the fairly frequent occurrence of pituitary adenomata in this disease. But in view of what has been suggested above—namely, that the pituitary lesion might be one expression of a general glandular involvement—it may not be coincidence only that pituitary adenomata were present in 6 out of 10 cases of carcinoma of the rectum, while in approximately 7 out of 10 cases (25 out of 33 actually) of this type of carcinoma, adenomata of the rectum were present before malignant changes supervened (Dukes [14]). Thus the incidence of pituitary adenoma and of rectal adenoma in cases of carcinoma of the rectum is very nearly the same.

THE NATURE OF THE PITUITARY ADENOMATA

Of the 280 pituitaries collected, nearly half of which have so far been cut in serial sections, 39 were found to contain an adenoma. In all but two the adenoma was composed of chromophobe cells or almost entirely of chromophobe cells, for careful searching will often reveal the presence of one or two cells of other types.

There were two very small adenomata of the acidophil cells of the pituitary—one in a case of carcinoma of the rectum and the other in a case of carcinoma of the bronchus, and neither showed any of the classical signs of acromegaly, or even of gigantism.

No adenoma of the basophil cells was seen but, in a case of carcinoma of the colon in a female 69 years old, there was an adenoma-like collection of those basophil cells which are frequently seen passing back into the posterior lobe from the region of the cleft.

There were two instances of a secondary deposit in the pituitary. The malignant growth in one case was a carcinoma of the bronchus, and in the other a lymphosarcoma.

Most of the adenomata seen were too small to give rise to symptoms, and it was only possible to diagnose one of the 39 clinically. But not every large adenoma gives an indication of its presence. One adenoma, nearly double the size of a normal pituitary, had remained symptomless even though it had grown out of the pituitary fossa. Presumably, in pushing its way backwards and outwards between the posterior clinoid process and the internal carotid artery, it had met with no resistance from structures which give rise to symptoms on being disturbed.

SUMMARY

The incidence of adenoma of the pituitary gland was approximately :—

(*a*) 10 per cent. in all cases.
(*b*) 44 per cent. in cases of carcinoma of other glands.
(*c*) Over 50 per cent. in cases of :
adenoma of the prostate gland ;
carcinoma of the pancreas ;
carcinoma of the rectum ;
carcinoma of the bronchus.

The majority of these pituitary adenomata (38 out of 39) gave rise to no known clinical signs or symptoms.

I am grateful to Prof. G. W. Nicholson and Dr. Dorothy Russell for checking my results ; and to Dr. A. A. Osman, Dr. P. P. Laidlaw, the Medical Research Council, the Clinical Research Committee of Guy's Hospital, and particularly to an anonymous donor, for their help.

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SIMPLE FIXTURES ADAPTING A TABLE FOR CRANIAL OR SPINAL OPERATIONS

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THE fixtures here described allow a table ordinarily used for general surgery to be modified, in a simple way, for operations on the skull or spine. The advantages of these fixtures are shared by the anæsthetist and the surgeon.

THE FACE-DOWN FIXTURE

Tables used at present for spinal or cerebral operations in the face-down position usually have supports for the patient's shoulders, which project up from the top of the table itself. The patient's forehead, on the other hand, rests at a distance from the table determined by the length of his neck. If the neck is short his mouth and nose touch, or almost touch, the end of the table. This unfairly cramps the anæsthetist during the long sessions of cranial surgery and puts a sore tax upon his skill. The surgeon, for his part, is often, as I know, constrained to fit long or short patients to a fixture of average size.

The new fixture removes both difficulties. (1) It eliminates neck-length as a cramping factor by supporting the patient's shoulders at points beyond the end of the table ; his face lies then still further off, and gives the anæsthetist full access to the mouth and nose. (2) It can be easily adapted to all patients, whether small infants or the largest men.

The face-down frame (*Fig. 1*).—A rigid metal frame fits into the slots that ordinarily carry the foot-piece of the Thackray table. On each side of the frame there is a short transverse bar which can travel backwards or forwards, and each short bar carries a crutch-like shoulder-support. The six-inch gap between these bars gives clear access to the face of the patient, however short his neck, while their mobility backwards and forwards allows adjustment for every length of trunk.

The shoulder supports are fixed in height, and each can slide in or out along its short bar according to the patient's width of shoulder. The supports have *curved* stems and are reversible. At their widest, when the stems diverge, they fit the very broadest individuals ; when reversed and close together they fit the smallest child. They can at once be adjusted to any patient of intermediate width.

The head-rest.—The front of the frame carries the head-rest—a semicircular, malleable band padded with sponge rubber ; it is fixed to a stout horizontal bar that slides through a vertical one, and can thus be moved backwards, forwards, or vertically ; a thumb-screw

makes it fast. The bars that carry the head-rest are long enough to permit adjustment for any length or inclination of the neck. Two sizes of head-rest have been found sufficient; both are hinged to the horizontal bar in such a way that the angle they form with it can be varied at will.

Rests for the patient's wrists keep the upper limbs alongside the trunk; the arms otherwise hang vertically.

Position of the table.—For the face-down posture the top of the table may be pumped to its maximum height of 40 inches or, if the surgeon prefers to operate with the patient's head well raised above the level of the trunk, the whole table is tilted and then brought to any height that is convenient for access. The surgeon and the assistant stand on stools.

The anæsthetist on a low seat with his back to the table has plenty of head-room beneath the frame. In front of him, below the support for the patient's head, is a shelf for bottles and instruments. Stainless steel hooks are provided to hang on the frame for the purpose of taking a sphygmomanometer dial or a tongue-forceps; a larger adjustable hook forms a convenient rest for the arm of the anæsthetist (Fig. 2).

FIG. 1.—The face-down fixture, showing the frame which fits into the ordinary foot-piece slots of the table. The frame carries shoulder supports with curved stems, and a head-rest; both are adjustable to patients of every size. Note the anæsthetist's shelf and arm-rest.

FIG. 2.—The face-down fixture in use. The anæsthetist beneath the frame has ample head-room and easy access to the patient's face. Note the wrist supports.

THE FACE-UP FIXTURE

The second fixture (Fig. 3) was designed in the first place to give free access—from beneath—to the back of the skull. Its primary purpose was to remedy a disappointing feature of the ventriculographic puncture, in which an outflow of cerebro-spinal fluid that begins well may often stop after the substitution of only a few cubic centimetres of air.

FIG. 3.—The face-up fixture arranged for ventriculographic puncture. The surgeon rests his elbows on the arm-table, which is adjustable in height. The head-supports allow free access to the neck of the skull.

Apart from the accident of displacing the needle's point from the ventricle the cerebro-spinal outflow fails, I believe, because the needle is often introduced posteriorly when the head is lying more or less on its side; the needle does not therefore enter the bottommost part of the ventricle. Obviously, however, the only sure way of aspirating all the fluid from a closed sac and replacing it with air is to puncture the sac at the bottom, and nowhere else—a thing difficult in the cerebral ventricle without a special support for the head.

Construction.—The face-up fixture consists of a frame, concave upwards, which fits, like its face-down fellow, into the foot-end of the Thackray table; it carries two narrow crescentic supports, which can be made to grasp any skull on either side, just behind the mastoid process. The surgeon, seated on a stool and working from below, has then a wide field between the crescents for tapping the ventricle at the lowest possible level. A convenient arm-table steadies and supports his elbows.

The face-up fixture is used for (*a*) frontal, and (*b*) parieto-temporal craniectomy.

(*a*) For frontal exposures the head lies face up as it does for ventriculography.

(*b*) For a wide parieto-temporal approach one crescentic support is adjusted beneath the head to the occiput; the other, set nearly at right-angles to the first, passes obliquely above and close behind the ear, supporting the parieto-occipital region on the side opposite the field of operation. The pivotal points of the two supports should be kept close together when adjusting them for this exposure.

THE PERINEAL SADDLE

Lastly, and at the suggestion of my friend Mr. Adams McConnell, a perineal support, shaped like a bicycle saddle, has been added to the table. This support, together with a pair of foot-rests, is easily slid on to the ordinary fittings of the table; it prevents all risk of the patient slipping down from the reversed Trendelenburg position required for many intracranial operations. The saddle is adjustable to patients of different length, and is also reversible for use in the face-up or face-down postures.

My best thanks are due to Messrs Thackray, of Leeds, who have made the fixtures from my design, and to their experts, Mr. Beardmore and Mr. Blackburn, for their admirable coöperation.

MEDICAL SOCIETIES

ROYAL SOCIETY OF MEDICINE

SECTION OF MEDICINE

At a meeting of this section held on March 27th the chair was taken by Sir FARQUHAR BUZZARD, the president, and a discussion was held on recent advances in the

Pathology and Treatment of Lymphadenoma

Dr. MERVYN GORDON, dealing with the pathology, said that lymphadenoma occupied an intermediate position between granulomata of known ætiology and malignant disease, and the problem of its causation might therefore be a key position to the problem of sarcoma. In a typical case the diagnosis could be made from sections of an enlarged gland, when the three characteristic changes were present: fibrosis, giant cells, and eosinophils. In practice, however, one or more of these three changes was often lacking. There were probably a number of different conditions, largely hitherto undifferentiated, in these atypical cases. The term "Hodgkin group" was a convenient one for the series of gradations between typical lymphadenoma and typical lymphosarcoma. The course of the disease was very suggestive of an infective agent, but the uniform fatality resembled malignant disease. So far lymphadenoma had not been certainly identified in or communicated to animals. It seemed possible that the ætiological agent would prove to be more nearly allied to that of sarcoma than of the granuloma-producing agents.

Recent work at St. Bartholomew's Hospital had included search for a pathogenic factor in lymphadenomatous glands by microscopical and other studies and work on allergic tests. No evidence had been found of spirochætal, tuberculous, or mycotic infection. Twort had found that lymphadenoma gland suspensions might cause local inflammatory nodules when injected into guinea-pigs; this had been confirmed and some very pronounced reactions noticed. In one case serial passage of this local subcutaneous granuloma had been obtained through eight guinea-pigs, the material being sterile throughout. Unfortunately this reaction could not be produced invariably.

A virus causing lymphogranuloma inguinale had been demonstrated by means of cerebral inoculation, and this procedure had therefore been used to investigate lymphadenoma. An encephalitis, frequently fatal, had been produced in the rabbit and guinea-pig, though not in the mouse or monkey, by inoculation of gland suspensions. After one to seven days susceptible animals showed symptoms such as fits, salivation, tremor, head-turning, and paresis, but the characteristic condition was one of incoördination and ataxia with muscular rigidity and spastic gait, occasionally also opisthotonus. Dr. Gordon showed slides and a film illustrating this condition. Application of this test to diagnosis showed 30 positives and 5 negatives during the last three years. Glands from other conditions gave negative results. The reaction could be obtained after heating the material for 30 minutes to 65° C. The test was of chief value in early cases; it might be negative with glands from chronic cases. The strongest reaction appeared when all the cardinal histological changes were present in the glands.

The active agent thus obtained was inactivated by keeping for half an hour at 80° C. and apparently increased when a suspension was kept by autolysis of cells. It was filtrable and withstood antiseptics well, but was gradually attenuated by ether. Moderate doses of X rays did not inactivate it. Successful passage had not been obtained, but there was evidence for the existence of both passive and active immunity, though both were very difficult to obtain. The agent was not likely to be a proteolytic enzyme. It might be complex and partly derived from the cells. An encephalitogenic agent was present in marrow and pus, but this did not invalidate the diagnostic value of the rabbit test. Bodies closely resembling the elementary bodies (Paschen) of vaccinia were found in large numbers in suspensions of lymphadenoma glands. No evidence of specific allergy had been obtained.

Dr. A. E. Gow said that the term lymphadenoma did not denote a single disease but several morbid processes which showed minor differences in clinical characteristics, course, prognosis, and therapeutic response. The histological changes were found in the reticulo-endothelial cells of lymphoid tissue, and both endothelial and reticulum cells showed overgrowth. Mononuclear elements obscured the normal structure of the gland. Endothelial cells gave rise to the typical giant cells, but in some cases mononuclear cells predominated, and there was no fibrosis and few giant cells. Considerable laboratory support was available for the theory that lymphadenoma was a virus infection, but clinically the condition did not resemble any other virus disease except oriental bubo (lymphogranuloma

inguinale) and perhaps psittacosis. Specific treatment had so far proved unsuccessful. Chicken serum had been tried, and also a suspension from the patient's own glands. The latter seemed to contain some active agent, as its injection was followed by temporary relief of pruritus and swelling of the nodes in face and neck. Dr. Gow described the technique of treatment and the course in several cases, and also the attempts made to diagnose Hodgkin's disease by an intradermal allergic test. The great majority of tests had given negative results, but in three instances where the disease seemed to be "resting" a small local reaction had been seen. He also showed a number of slides illustrating the histology. There could be no doubt, he said, that life was prolonged by irradiation, and the periods of remission were increased in length, and patients were able to resume their occupation, apparently well.

A paper by Dr. W. M. LEVITT was read by Dr. R. F. PHILLIPS. The radiologist, he said, wanted to know from the physician what to treat. Further progress could only result from coöperation. A localised focus could be made to disappear, almost for certain. The doses were considerably below the tolerance limit of healthy tissues and much might be lost by attempting to use larger doses. Any increase should be in the number of areas treated. Histologically as well as clinically the lesions disappeared, but the disease was not cured. Recurrences appeared, and sooner or later became so widely disseminated in chest and abdomen that adequate doses could no longer be applied. Nevertheless palliative treatment could still be used; pressure symptoms and early cachexia could be relieved. In the final stages the disease became more resistant to X rays. Almost magical in early stages, X ray treatment might be worse than useless in the late stages. The palpable mass was not necessarily the original focus, which might really lie in deeper tissues. An initial lesion which escaped treatment would act as a centre for spread. The disease required study from the angle of distribution and march. Finzi taught that the mediastinum should be treated in every case, whatever the apparent lesion, but the abdomen presented a more difficult problem because of the effects of X rays on the organs. It was arguable that the abdomen ought to be treated as a routine measure. The chief palliative measure was the "X ray bath," an exposure of wide areas to repeated small doses. Radiologists now knew the dosage for "baths" of all areas except the trunk, where there was still some danger of leucopenia. The results of abdominal baths had so far proved only temporary.

Prof. U. FRIEDEMANN suggested that there might be two agents, one producing the encephalitis in rabbits and the other the allergic skin reaction. He had found that normal bone-marrow injected cerebrally produced the same picture, and thought more depended on the site of injection than on the material injected.

Dr. C. E. VAN ROOYEN mentioned some of the many clinical conditions described by Hodgkin. The biological test was one of the greatest value, which had been confirmed in Edinburgh and Glasgow. A gland which contained very large numbers of leucocytes gave a persistently negative reaction and the specificity of the test seemed clear. The parasite seemed to be intracellular; the reaction was produced by something that was coming out of a cell. It might be a living agent, a toxic product, or a ferment. In the absence of inclusion bodies and animal transmission it could not be called a virus. But neither typhoid, leprosy, nor syphilis had ever been satisfactorily transmitted to animals. He thought it was a toxin. Virus infection in a cell might cause degeneration and death or proliferation; lymphadenoma was a proliferative phase.

Dr. F. PARKES WEBER offered another explanation of Hodgkin's disease; he did not believe that the evidence for infection was by any means conclusive, and thought there was just as much to be said for the neoplastic theory. By neoplastic disease he meant a proliferation which served no useful or conservative purpose to the organism and for which no causative agent had been discovered. It might be benignant or malignant. The myeloses were malignant proliferation of the leucopoietic system of the body. Erythræmia was benignant proliferation of the erythroblastic system. Hodgkin's disease was, perhaps, a more or less malignant proliferation of the reticulum—a reticulomatosis. It was characteristic of neoplastic cells that they could continue their ordinary work to some extent. The reticulum was able to form all the cells found in every type of Hodgkin's disease.

MEDICAL SOCIETY OF LONDON

A MEETING of this society on March 26th, with Mr. R. DAVIES-COLLEY in the chair, was devoted to a discussion on

Functional Disorders of the Bowel

Dr. T. L. HARDY (Birmingham) pointed out that many of the terms applied to colon dysfunction—such as visceroptosis, muco-membranous colitis, atonic constipation, and colon spasm—were inaccurate and needed revision, though they indicated that the neuromuscular imbalance of the bowel had a variety of phases. The tone, coördination, and harmony of the intestinal movements depended on the extrinsic autonomic nervous system; the sympathetic fibres were inhibitory to the bowel and caused contraction of the sphincters, while the parasympathetic was predominantly motor and inhibited the sphincters. Physiologists, however, held that these nervous influences were affected to some extent by the state and tone of the muscle at the time. Further knowledge of this subjec could be expected not from animal experimentation but rather from operations on the sympathetic nervous system and observations on the effects of such drugs as atropine, adrenaline, and acetylcholine.

The functional disorders of the colon could be regarded as due to an imbalance between the nervous and the muscular apparatus, which resulted in disturbance in mechanical and secretory activities—a disturbance made known to the patient by symptoms such as abdominal discomfort or pain, distension, and the abnormal elimination of fæcal material. Often there was a psychical or emotional factor in addition. It was hard to estimate the frequency of these disorders, especially as the intestinal neuroses diminished in frequency with descent of the social scale. At Birmingham General Hospital, out of 1078 patients admitted on the medical side for chronic disorders of the digestive system, there were 85 of colon dysfunction (8 per cent.), but E. I. Spriggs, and Jordan, of New York, published figures giving a much higher proportion. Of 157 patients treated by the speaker 89 were females and 68 males; the greater proportion were in early middle life, 51 being

aged 31–40, 29 41–50, and 27 21–30. Some of the late results of dysenteric and non-specific inflammations seemed to be due to an irritability of the neuromuscular mechanism, and were periodically made evident by attacks of diarrhœa; also chronic disease of the gall-bladder and appendix commonly caused reflex disturbances of colon function, and thus provided a good many diagnostic difficulties. Similarly an inflamed Fallopian tube or ovary might set up spasm in an adjacent coil of bowel, and influenza and upper respiratory disorders might play a part. Achlorhydria as a predisposing cause of disorders of the colon was rare, but dietetic factors were important, and some of the modern food cults did not encourage healthy action of the bowel. The colon dyspeptic reduced his total intake to relieve his indigestion, but he really aggravated it by increasing his constipation. The chief rôles in causation must be assigned to constipation and its treatment by excessive purgation, and to nervous instability. Constipation was complained of by the vast majority of patients—e.g., by 106 of his 157—77 of whom were taking irritant aperients daily. The drugs most commonly used were vegetable laxatives, such as rhubarb, aloes, cascara, and senna, and the synthetic product phenolphthalein, the last of which seemed especially harmful, since it was in part absorbed and excreted in the bile, and might go on acting over three or four days. Its continued use resulted in the passage of much mucus, and sometimes in hæmorrhoids.

Emotional upset and fatigue were common causes of functional disorder of the colon, as also were cold winds and tobacco. Abnormal mental reactions characterised many of the patients, especially tall thin people, and there was often a vicious circle of constipation, neurosis, purgation, indigestion, and undernutrition. There was no experimental evidence that chemical or bacterial toxins were absorbed from the colon in intestinal stasis in amounts sufficient to cause symptoms, and many so-called toxic symptoms were the reflex results of distension of the sigmoid and rectum with fæces. Food allergy was very real, but there was danger in too facile diagnosis of it.

Dr. THOMAS HUNT said that of 93 cases of simple indigestion without organic lesion, he had been able to place 62 in the category of irritable spastic colon. Even severe cases might show little on X ray examination or by ordinary physical investigation; on the other hand, there might be big displacements with normal function. Certain symptoms aided the differential diagnosis. An increased frequency of discomfort in cold weather, and backache, were both common, as was also aching in the muscles after the passage of mucus. Flatulence was frequent and true aerophagia occurred in 11 of 53 cases; patients often said they had the feeling that defæcation was always incomplete. Frequency of micturition was another symptom, and a full bladder could excite colon spasm, thus accounting for the pain which sometimes awakened a patient at night. There might be loss of weight and vomiting, sometimes severe, and these might be aggravated by injudicious handling from the psychological point of view. Three main points of tenderness were the right iliac fossa (over the cæcum), the epigastrium (over the aorta), and the left iliac fossa (over the sigmoid).

The causes could be considered under four heads: reflex, bacterial, allergic, and nervous. The most important, he thought, were the nervous; even the effects of taking purgatives must be placed second to them. It was possible to exaggerate the importance of bacterial infection, and this had the disadvantage of fixing on patients the idea of a physical illness. Actually a sea voyage with congenial companionship (to take one example) might be far more useful than vaccines and other remedies directed towards the physical condition. Even in the cases attributed to over-use of purgatives there was a strong nervous element; this was shown by the fact that of 75 patients with other than digestive disorders, 37 had been taking purgatives every night for ten years or longer but were not adversely affected. The emotional element could sometimes be greatly reduced by reassurance, explanation, and argument, apart from any intricate psycho-analysis. The most important cause of the trouble was fear. The fear of organic disease was fairly common. At the same time there were other sources of anxiety, associated, for example, with masturbation, sexual frustration, or coitus interruptus. Lack of work and the state of mind it produced could not be ignored.

In treating the unstable colon the diet should be as free as possible, the only restrictions being the exclusion of substances with hard residue, such as nuts and peel. It was desirable to limit the formation of gas in the bowel, and a mixture of belladonna and bromide was often successful, though belladonna had less effect on colon spasm than on pyloric spasm. Sedatives lessened fear and nervous tension. In some cases he had found nitrites of value; amyl nitrite capsules almost always brought temporary relief. He had not seen much effect experimentally from either adrenaline or pilocarpine. In cases of loss of appetite and under-nourishment insulin might be useful, for a gain in body-weight would give valuable encouragement.

Dr. A. F. HURST said it was important to realise the essential part played by mucus as a lubricant; it was absurd to look upon its presence in the stools as evidence of colitis. Secretion of mucus took place whenever the colon was irritated, and an aperient stimulated secretion in excess; but this excess should not be regarded as evidence of disease unless it was associated with looseness of bowels not caused by aperients. In normal defæcation the whole colon took part, even the cæcum, and most cases of constipation were due to deficiency in the process. Defæcation was a conditioned reflex, initiated when the child was first required to regularly use the chamber; if this reflex was for any reason broken in later life the habit should be re-formed, and this often sufficed to cure the constipation. He considered that there was only one sphincter of the colon—namely, the anal. It was the easiest of the sphincters to get at; it could be easily dilated by the fingers, and in Hirschsprung's disease frequent digital dilatation was often effective without the operation of sympathectomy. Intestinal allergy was rare but very important. Patients with this had a sudden violent colic, with diarrhœa and a feeling of unfitness; they often gave a history of asthma or hay-fever, and the blood always showed eosinophilia during the attack. Adrenaline sometimes cut short the attack. Intestinal flatulence Dr. Hurst attributed to irregularity in the small intestine.

Dr. G. E. VILVANDRÉ spoke of the value of barium meals and barium enemas in disorders of the colon. No barium meal examination was complete, however, unless a radiogram was seen also after defæcation. If organic disease was present there might then be contraction of the colon.

Mr. EARDLEY HOLLAND said that many women with functional disorders of the colon were thought

to have gynæcological lesions. Most of the cases of this kind which he saw were the products of some emotional upset. Retroflexion of the uterus was very common indeed, and suspension of the uterus gave the patients hope. Enuresis and dyspareunia also were found in cases with colon disturbance.

Dr. CAMPBELL MCCLURE said that some people seemed to have an inborn imbalance of the vago-sympathetic system. He had often found tachycardia and similar disturbances in association with colon trouble.

Mr. W. MCK. MCCULLAGH did not think that uterine retroversion caused intestinal disorders; but a train of symptoms, including indigestion and dyspepsia, might be caused by the pressure of the uterus on the ovaries, and he had seen women cured of indigestion by ventro-suspension.

Dr. C. E. NEWMAN said that the emotional element in these cases had formerly been much neglected. When investigating functional disorders of the biliary tract it was borne in upon him how often these patients complained of disorders of the colon. Intolerance of physical cold, pain over the gall-bladder region, backache, nausea without vomiting, and respiratory signs, such as sinus arrythmia, were all commonly found. It was important to give due place to vagal action in these cases.

Dr. J. E. A. LYNHAM drew attention to the great variety in colons as revealed by X rays. Patients with undescended cæcum and a rectocæcal appendix showed a peculiar picture of colon upset. They did not have periodical attacks, and they might go on without disturbance for months or years; after which there would be an attack of great pain, with distension and constipation.

Dr. HUNT, in reply, said he wished to make it clear that he did not conclude that colon disorder was functional until a thorough examination had been made to exclude organic disease.

EDINBURGH OBSTETRICAL SOCIETY

A MEETING of this society was held on March 19th, with Dr. OLIPHANT NICHOLSON, the president, in the chair.

Contraction of the Uterus

Dr. CHASSAR MOIR read a paper entitled Recording the Contractions of the Human Pregnant and Non-pregnant Uterus. His observations were made with three types of apparatus: (1) an intra-uterine bag and recording manometer by which contractions of the puerperal uterus could be recorded; (2) an abdominal apparatus which recorded changes in the shape of the uterus; and (3) an intra-uterine bag which could be used in the non-pregnant uterus. It was found, he said, that suckling usually caused strong contractions of the puerperal uterus to appear. Ergotoxine, ergotamine, and the alleged new alkaloid sensibamine all caused strong contractions of the uterus, but there was a delay of half an hour or more before any effect was seen after intramuscular injection. This lessened their value in post-partum hæmorrhage unless they were combined with a quick acting drug. Histamine was not effective because it had a negligible action on the uterus when it was used in doses small enough to avoid unpleasant flushing effects. Pituitary extract was reliable early in the puerperium, but its action was very erratic after the first week; in the late puerperium it often failed to produce any activity of the uterus. Liquid extract of ergot (B.P. 1914 and also B.P. 1932) had a powerful quick action on the uterus, the effect sometimes appearing in as short a time as four minutes when it was given by mouth. It caused marked spasm of the uterus for an hour or longer, its action being entirely different from that of the ergot alkaloids, and it was this quick acting factor in ergot which led to its use by midwives 200 years ago. Intra-uterine injection of glycerin was not an effective means of causing uterine contractions.

By a double uterine apparatus contractions were simultaneously recorded from fundus and cervix. There was some evidence of a peristaltic wave in the uterus, since the contractions of the cervix lagged about 17 seconds behind those of the fundus. The non-pregnant uterus showed contractions at all periods of the menstrual cycle, but these gradually increased in force from the sixteenth day till the onset of menstruation. During menstruation the contractions exerted a pressure considerably in excess of that seen during parturition. In a case of dysmenorrhœa the intra-uterine pressure rose to surprising heights. Contrary to Knaus's observations published in 1929, it was found that the uterus always responded to pituitary extract. Oxytocin (Pitocin) in doses of 10 units intramuscularly had no effect on the non-pregnant uterus, whereas vasopressin (Pitressin) in the same dose had a very marked effect.

INFECTIOUS DISEASE

IN ENGLAND AND WALES DURING THE WEEK ENDED MARCH 24TH, 1934

Notifications.—The following cases of infectious disease were notified during the week: Small-pox, 5 (last week 10); scarlet fever, 3093; diphtheria, 1189; enteric fever, 19; acute pneumonia (primary or influenzal), 1529; puerperal fever, 70; puerperal pyrexia, 110; cerebro-spinal fever, 17; acute polio-myelitis, 5; acute polio-encephalitis, 1; encephalitis lethargica, 4; dysentery, 15; ophthalmia neonatorum, 96. No case of cholera, plague, or typhus fever was notified during the week.

The number of cases in the Infectious Hospitals of the London County Council on April 1st–2nd was as follows: Small-pox, 17 under treatment, 1 under observation (last week 16 and 0 respectively); scarlet fever, 1637; diphtheria, 1803; enteric fever, 7; measles, 3557 (last week 3470); whooping-cough, 325; puerperal fever, 21 mothers (plus 7 babies); encephalitis lethargica, 260; poliomyelitis, 4; "other diseases," 160. At St. Margaret's Hospital there were 19 babies (plus 11 mothers) with ophthalmia neonatorum.

Deaths.—In 118 great towns, including London, there was no death from small-pox, 2 (1) from enteric fever, 187 (82) from measles, 14 (2) from scarlet fever, 37 (9) from whooping-cough, 54 (7) from diphtheria, 58 (23) from diarrhœa and enteritis under two years, and 109 (26) from influenza. The figures in parentheses are those for London itself.

The weekly total of fatal cases of influenza is a little lower, the figures for the last few weeks (working backwards) being as follows: 109, 115, 99, 96, 85, 87, 73. The fatal cases were widely distributed among 49 great towns, the highest number of deaths being reported from Birmingham 10, Leeds, Liverpool, and South Shields each 7, York, Stoke-on-Trent each 3.

There were 16 fatal cases of measles in Liverpool, 12 in Middlesbrough, 10 in West Ham, 4 each in Walthamstow, Salford, and Norwich. Whooping-cough caused 6 deaths in Birmingham, 3 in Liverpool. Seven deaths from diphtheria were reported from Leeds and Liverpool, 4 from West Ham and Birmingham, 3 from East Ham and Hull.

The number of stillbirths notified during the week was 282 (corresponding to a rate of 43 per 1000 total births), including 42 in London.

LANCASTER ROYAL INFIRMARY.—Last year this hospital derived £1954 from the payments of 149 private patients. There were 1816 in-patients, who stayed on an average 19·14 days, as against the previous year's average of 17·28 days.

REVIEWS AND NOTICES OF BOOKS

Traité de médecine des enfants

Publié sous la direction de P. NOBÉCOURT et L. BABONNEIX. Secrétaires de la Rédaction: J. CATHALA et J. HUTINEL. Paris: Masson et Cie. 1934. Tome I. Pp. 884. Fr.170. Tome II. Pp. 960. Fr.150. Tome III. Pp. 1088. Fr.170.

IT is nearly 25 years since a system of pædiatrics in any way comparable with the present one has appeared in France. These three volumes are the first of five, and the work has been entrusted to over 70 authorities. The first volume begins with a historical review of pædiatrics and pædiatricians from the time of Hippocrates to the present day, and includes such illustrations as the obtaining of asses' milk for artificial feeding, the method of leaving and receiving infants in a foundling institution, and (a more modern touch) a royal visit in 1790 to a ward in a children's hospital. The aims and methods of prophylaxis and treatment are outlined in some detail. The main body of the volume is devoted to a consideration of normal and abnormal growth, development and nutrition, endocrine disorders, congenital abnormalities, and deficiency diseases. The disorders of growth are particularly well illustrated, though a more liberal use of normal controls in the photographs would have made the significance of these more plain. In a work of this scope, a rather fuller discussion of the recent work on the pituitary might perhaps have been usefully included, though the endocrine section otherwise gives a fair presentation of the stage that has been reached by careful clinical rather than experimental observation.

The second volume deals with infectious diseases and diseases of the blood and hæmopoietic system. We note that rheumatism is included without comment amongst the infectious diseases, although the theory of a streptococcal origin is rather summarily dismissed. Those with long memories may echo the author's opening comment: "Il serait vain et peut-être cruel de rappeler tous les germes qui ont été tour à tour décrits dans le rhumatisme articulaire aigu." "Fourth disease" receives full recognition, but (a little in the grand manner) a fifth and sixth disease as well. Congenital syphilis is, as would be expected, fully and admirably discussed, though few British clinicians will accept the attribution to it of such widespread effects; indeed, those who boggle at inheritance as far as the third generation will be a little staggered by its calm visitation on the children of the fourth and fifth.

Diseases of the cardiovascular and respiratory systems, and the first part of the section devoted to diseases of the alimentary tract, are included in the third volume; the numerous X ray pictures are well chosen and for the most part well reproduced, though, as is so often the case, those in which lipiodol has been used entirely fail to give adequate contrast in the print. It is perhaps a pity that in view of the value of lipiodol in the diagnosis of pulmonary disease in childhood, and the pioneer work that has been done in France in this field, more space was not devoted to a description of the technique of its injection and to the dangers and difficulties to be avoided in its use. The section on pulmonary tuberculosis in childhood gives an excellent review of the modern conception of the pathology and spread of the disease.

The volumes are beautifully produced and profusely illustrated, but in a work of such dignity more attention should have been paid to the accuracy of the references. A very great number of the English and American proper names are spelt wrongly or inconsistently (in one instance there are four mistakes in five names, and three variations of one name on one page); the authors of one section give naked-eye and histological post-mortem findings in a case quoted from the English literature which is, to our certain knowledge, still alive and in excellent health. The work as a whole, however, is a real addition to pædiatric literature, and the appearance of the subsequent volumes will be awaited with keen interest.

Hypnosis and Suggestibility

By CLARK L. HULL, Professor of Psychology, Institute of Human Relations, Yale. London and New York: D. Appleton-Century Company Inc. 1933. Pp. 416. 15s.

Hypnotism—Friend of Man

By J. LOUIS ORTON. London: Thorsons. 1933. Pp. 280. 5s.

Hypnosis and Suggestion

By WILL. F. LOVATT, C.S.M.M.G., B.P.A. London: Rider and Co. 1933. Pp. 144. 2s. 6d.

Hypnotism Explained

By ALAN MACEY, M.D. London: Ferland Press. 1933. Pp. 131. 2s.

HYPNOSIS is not only a therapeutic instrument for treating certain abnormal mental states; it is still more a mental state, which provides material for investigation not only by the psychologist, but by the neurologist. To the former, it is important in the understanding of suggestion, dissociated mental states, and hysteria. To the latter, it has affinities with narcolepsy, catalepsy, and allied phenomena related to the sleep mechanism and perhaps to the epilepsies.

Dr. Clark Hull's work on hypnosis is of extreme interest as one of the very few attempts that have been made to deal with the phenomena by the controlled methods of experimental psychology. After describing concrete experiments on methods of inducing hypnosis and negative and positive states of suggestibility, he gives details of laboratory experiments which are of great value in illustrating how these illusive and much-distrusted phenomena are accessible to laboratory technique. Post-hypnotic phenomena are carefully studied, and most important is the author's denial of the identity of sleep and hypnosis. Hypnosis as heightened suggestibility is experimentally demonstrated, and such an important topic as non-prestige suggestion is analysed and related to perseveration. No psychopathologist can ignore this carefully planned inquiry.

Beside this treatise the books by Orton and by Lovatt are merely pleasant and popular expositions of hypnosis as universal panaceas. Both are well-endowed practitioners of the art, and Orton in particular writes in a friendly diffused manner which to the suggestible may have quite a hypnotic effect producing perhaps, in consequence, some uncritical enthusiasm.

Dr. Macey provides in small bulk a practical exposition of hypnosis with none of the faults exhibited by those of Orton or Lovatt. It is strictly medical and describes methods of induction and the application of hypnosis to medicine, surgery, and education. The author describes the relation of hypnosis to multiple

personality, quoting Morton Prince's case. He omits, however, to discuss this case in the light of general psychopathology. This is indeed an error common in books devoted exclusively to hypnosis as an isolated phenomenon, and generally speaking provides an argument against its separate consideration.

Oxidation-reduction Potentials in Bacteriology and Biochemistry

Second edition. By L. F. HEWITT, Ph.D., B.Sc., A.I.C. Published by the London County Council. 1933. Pp. 81. 2s.

THIS valuable little monograph, the first edition of which was reviewed in our columns three years ago, was published by the London County Council as a combined description of original work carried out in their laboratories, and an introduction to the basic principles involved. The venture has had a gratifying success, which is due to the straightforward manner in which the author has dealt with his intricate subject. In this edition the text has been thoroughly revised, recent work has been included, and the bibliography has been brought up to date. Though no sensational advances are recorded, steady progress has been made. Oxidation-reduction potentials have come to stay in bacteriology and biochemistry, and this little book provides an excellent introduction to this study.

Cutaneous Neoplasms

By C. NORMAN PAUL, M.B., Ch.M., Physician for Diseases of the Skin, Sydney Hospital; Past President, N.S.W. Branch of the British Association of Dermatologists. London: H. K. Lewis and Co., Ltd. 1933. Pp. 153. 10s. 6d.

THE prevalence of skin carcinomata and precarcinomatous changes (keratoses on the exposed areas) in the inhabitants of Australia is well known, and has been emphasised by Dr. Paul on more than one occasion in the past. It is equally true that, per contra, lupus and tuberculous infection of the integument is rare, and there is little doubt that the power of the sun is to be blamed for the one and thanked for the other. Dr. Paul takes occasion to warn his compatriots of the dangers incurred by sun-bathing, which, superimposed on the unavoidable exposure, may turn the balance in favour of malignancy at a later date. The warning need not be taken too seriously by sun-worshippers in this country, for to be dangerous exposure must be prolonged and frequently repeated, and the chances of such cumulative effect in our climate, or even in central Europe, are small.

All the commoner tumours, except the nævi, are here considered in detail, and most of them are illustrated by excellent reproductions of photographic studies, together with photomicrographs of sections in the more important group. A section has been devoted to a brief discussion of the seborrhœic and arsenical keratosis, xeroderma pigmentosum, and some of the peculiar abnormalities of the sweat and sebaceous glands, leading to neoplastic—not necessarily malignant—changes. By far the greater portion of the book, however, is concerned with malignant disease in its various forms, the rodent ulcer—or basal-celled carcinoma (both single and the rare multiple types)—the less common squamous varieties, and X ray epitheliomata. Here Dr. Paul's opinions should be read with particular respect, for there is probably no other living dermatologist who has had so extensive an experience. One new departure in treatment will doubtless be tried; for the author claims better results with the consecutive application of radium and CO_2 in certain types of growth—the raised nodular, the ulcerative lesion with raised nodular border, and the superficial with beaded border and cicatrising centre—than with either treatment alone. The freezing precedes the radium application for two or three weeks according to the depth of infiltration, or for so long as shall render the subsequent radium application effective in one session.

It was a good idea to incorporate cutaneous neoplasms in one volume, and the lucid and unpretentious way in which the material is dealt with should make a general appeal.

Food and Character

By LOUIS BERMAN, M.D. London: Methuen and Co., Ltd. 1933. Pp. 384. 8s. 6d.

IT is a somewhat humbling reflection that the human belief in magic is such that the last 500 years have simply served to substitute vitamins for mandrakes and gland extracts for love philtres. The title Dr. Berman gives to his first chapter—"Body-mind as a Chemical Brew"—is a good example of the fare his book provides, whilst an introductory cocktail is extracted from the dicta of Henry Ford, Senator Copeland, and others. As there are always a great many people who like to think their food fads are based on the profoundest scientific reasoning (and indeed Dr. Berman handles words like "purins" and "calcium balance" as a master), this book will doubtless appeal to a large public and have an extensive circulation.

A Text-book of Physiology

For Medical Students and Physicians. Twelfth edition, thoroughly revised. By WILLIAM H. HOWELL, Ph.D., M.D., Sc.D., Emeritus Professor of Physiology in the Johns Hopkins University, Baltimore. London and Philadelphia: W. B. Saunders Co., Ltd. 1933. Pp. 1132. 32s. 6d.

IN the preface to this book is to be found the sentence "It is doubtless the art of presentation that makes a text-book successful or unsuccessful." Dr. Howell is a master of this art as well as of his subject, and the latest edition of his work is no less attractive than its predecessors. The subject matter is presented in a straightforward way, with great ease of expression; yet no explanation is shirked which is necessary for its proper understanding. The book is not suitable for the advanced student or the research worker, since the author has himself sifted the available facts and theories and has aimed at placing a clear statement before the reader; it is, however, ideal for the student beginning his study of physiology and for anyone who desires a coherent framework on which to build future knowledge, be it on advanced physiology or on medicine. A generous sprinkling of footnote references furnishes jumping-off points for more detailed study if this is desired. The number of pages gives a rather misleading idea of the size of the book, since the print is large and the margins spacious; these features make for ease in reading, however, and the publishers deserve credit for an attractive production.

The arrangement of material is unlike that usually

found in English text-books, the central nervous system and special senses being treated in early sections; the former is well done, but is still dominated by the anatomical tradition. That the interests of the student are given first place is emphasised in the section on blood, where the subject of coagulation is dealt with lucidly; the author's own theories are not stressed at the expense of others. Digestion comes rather late in the book, and is described with a minimum of chemistry; much that often precedes digestion is discussed later in relation to kidney excretion, nutrition, and heat production, while the classification of proteins and a certain amount of physical chemistry are relegated to the appendix. This method has advantages from the point of view of interest and perspective, but the student who is a little weak in his preliminary sciences would probably appreciate an enlargement of the appendix to include at least the chemistry of carbohydrates and fats. A reference section of this sort would be extremely valuable, even at the risk of repetition, and would justify the fundamentally sound arrangement which has been adopted. Throughout the book, wherever there is danger of confusion of issues, a historical survey has been inserted, which makes clear at least the evolution of the subject. For the most part the illustrations have been carefully chosen, so that each has an unmistakable significance; they include a few very good colour plates.

Over den Oorsprong der Syphilis

By W. F. R. ESSED. Amsterdam: H. J. Paris. 1933. Pp. 328.

THE title of this book is somewhat misleading, for only a very small fraction of its space is devoted to the origin of syphilis. The author holds that the disease "has always been known in Europe." The evidence for this statement is not given in detail, but is summarised in the sentence: "The recognition by various ancient writers of condylomata lata as an infective lesion of the genitalia and anus, Hippocrates' description of the combination of perforated palate and saddle-nose, and the existence of pre-Columbian bones showing gummatous osteomyelitis are facts which cannot be explained away." The general consensus of informed opinion at the present day is opposed to the pre-Columbian existence of syphilis in Europe. The evidence on the other side has been well summarised by W. A. Pusey in his book "The History and Epidemiology of Syphilis," recently reviewed in these columns.

The bulk of the book consists in an attempt to show that the "new sickness" which was brought into Europe by Columbus' seamen on their return from Haiti in 1493, which within the next few years devastated Western Europe and to which Fracastor in 1530 gave the name of syphilis, was in fact not syphilis at all but frambœsia. The author lays stress on the clinical resemblances between the new sickness, or morbus gallicus, and yaws; on the similarity of the native names for yaws, in different parts of the world at the present day, to the names given to the "new sickness"; and on the differences between the latter and syphilis as now seen. The most interesting part of the book is the full description, compiled from contemporary sources, of the clinical characters of the "new sickness." The book would be improved by the addition of an index and by the arrangement of the extensive bibliography on some systematic plan.

HEALTH OF THE NAVY IN 1932

THE year was a healthy one in the Navy[1]; new cases of illness and daily sick were both less than in previous years. Accident was the chief cause of death, and the rate was substantially raised by the loss of 57 lives in Submarine M2; allowing for this, the death-rate of Army and Navy is almost identical—viz., 2·53. Fatal injuries (apart from the M2 disaster) numbered 66, suicide 14. From disease the death-rate was 1·57 per 1000, the chief contributants being pneumonia 18, pulmonary tubercle 12, malignant new growths 10. On the other hand losses by invaliding were greater by 112; pulmonary tubercle 194 (30 plus), sequelæ of gonorrhœa 32 (22 plus), "other nervous diseases" 73 (30 plus), mental instability 38 (21 plus). One of the 12 cases of enteric fever ended fatally; it is not quite clear from the report when preventive inoculation was given.

Malaria has slightly decreased; the majority of new cases were benign tertian, but in Africa only malignant tertian were seen. Prophylaxis by quinine is touched on: the men of *Delphinium* all took quinine and none got malaria, but the report gives no clue to the degree of exposure. Influenza was light; cases chiefly occurred at home. There were 6 deaths among 43 cases of meningococcal infection; deaths were halved though cases had increased. Some credit for this result is given to frequent lumbar puncture combined with glucose per rectum and much liquid by the mouth. Intrathecal injection of serum was continued until the cerebro-spinal fluid became clear, serum being also given intravenously (up to 40 c.cm. daily) if there was a rash. The incidence of pulmonary tuberculosis has increased from 2·05 to 2·47 per 1000, the highest rates being found on destroyer and submarine depôt ships, but the numbers are too small to draw deductions. It is however noteworthy that the incidence of tubercle in the Navy is double that in the Army or the Air Force at almost every age, a fact worthy of study by the Joint Medical Services Committee which is now in being. Undulant fever is raising its head again at Malta. Venereal diseases are no worse—syphilis slightly up, gonorrhœa slightly down—but, as we have seen, rather more invaliding for sequelæ of gonorrhœa. The prevalence of tonsillitis in Army and Navy is almost equal, but catarrh is almost three times as frequent as in the Navy. Scarlet fever in *St. Vincent* has been again halved by Dick testing and active immunisation. Of diphtheria there were 18 cases in Greenwich Hospital School, only four of which were clinically recognisable. Among the other diseases caused by infection were a fatal case of anthrax meningitis in England, and one of glanders in a Somali from the Red Sea.

Two cases of gastric ulcer, operated upon on the fifth and sixth days, made good recoveries without drainage. Antigonococcus vaccine was used with good results in chronic cases and in others with metastatic sequelæ. An artificer apprentice was found with dextrocardia, but in perfect health. An infra-red generator has been installed at Chatham, and has been usefully employed in obtaining deep hyperæmia. Eight cases of acute appendicitis and one of perforated duodenal ulcer were operated on successfully in ships at sea. Only eight men were invalided refusing operation, showing an increasing confidence of the service in its medical staff.

[1] Statistical Report of the Health of the Navy for 1932. H.M. Stationery Office. Pp. 144. 2s. 6d.

THE LANCET

LONDON: SATURDAY, APRIL 7, 1934

INCREASING CARE OF THE BLIND

THE Ministry of Health has done well to publish a revised edition of the handbook on the welfare of the blind compiled by its advisory committee.[1] The book is based on the definition of blindness adopted for the purposes of the Blind Persons Act of 1920; it deals with the register of blind persons which every county and borough council in England and Wales is under the obligation of keeping, and with the methods of certification for the purposes of these registers. It sets out the welfare services that have been established for the employable blind by way of training and augmentation of wages earned when trained; and for the unemployable blind, unfortunately in the majority, by means of Braille teaching and home visiting, including the measures to be taken to prevent any blind person from falling into destitution. A growing number of authorities are laying down a scale up to which the income of each unemployable blind person should be brought, and have voted substantial sums to assist the funds of voluntary agencies in meeting these payments. The first difficulty that arises in implementing this measure is on the definition of blindness. There are still two statutory definitions. One, for purposes of the Education Act, runs: "Too blind to be able to read the ordinary school books used by children"; the other, for purposes of registration and eligibility for certain privileges, including the old-age pension at 50, runs: "So blind as to be unable to perform any work for which eyesight is essential." In interpreting the latter definition certain rules have been laid down by the Ministry of Health for the guidance of the certifying surgeon. The main difficulty is to decide whether or not a person having visual acuity between 3/60 and 6/60, with full or nearly full fields of vision, is or is not blind within the meaning of the Act. There are a considerable number of these borderland cases, and some latitude is necessarily given to the certifying surgeon, certain points being laid down for his guidance. Cases with visual acuity between 3/60 and 6/60 should, if there is no material contraction of the field, not as a rule be certified as blind. If however there is a material restriction of the field they should. Does this mean that when one eye is blind or excised and the other sees, say, 5/60 with full field the case should not be certified? Here there is necessarily a restriction of the binocular field of vision, and probably many cases of this type are certified. The certifying surgeon is also told that he can take into account the age at which the defect of sight was first noticed and the age of the patient. Young persons can adapt themselves more readily than old to new conditions, and a man whose defect is recent is less likely to be able to adapt himself to any sighted work than one whose defect is of long standing. The problem of the partially sighted, such as some of those indicated above, does not come within the scope of this handbook, but until there is some consensus of opinion as to what should be done with them and how to help them there will always be the tendency to deal leniently with them in certification. This specially applies to those partially blind persons who, having been educated at a blind school and received a vocational training fitting them to earn their own living partially as subsidised workers under the Blind Persons Act, would yet be quite unable to support themselves without such aid.

All the 146 councils of counties and county boroughs in England and Wales have now made schemes under the Act. The first matter for which these schemes make provision is registration. At present this must be very incomplete. For instance, in 1932 the number of registered blind persons was 59,788. Of these the number under 5 years old was only 225, whereas the number between 5 and 16 was 2066. Now blindness which first becomes manifest during school age is rare, and it is probable that the great majority of the 2000 registered during school age were cases of blindness either congenital or occurring during infancy. It is true that blindness due to ophthalmia neonatorum, which used to be the most important cause in infancy, has very markedly diminished, but this is not the case with blindness due to various congenital malformations, such as congenital cataract, which form a large proportion of the whole. The fact probably is that the majority of cases of infantile blindness do not come to the notice of public authorities until they are of school age. Blind children of school age may be, and for the most part are, sent to day or residential schools at the cost of the local education authority, and are kept there until the age of 16. For high myopes and other children who are partially blind special schools and classes have been organised in London and some other centres, but most country children of this class are either accepted in a blind school or take their chance in an ordinary one. There are not enough of these special classes for the partially sighted. When a blind person is trainable for remunerative employment the Act provides that the local education authority shall secure adequate and suitable provision for this. Actually, this duty is discharged by subsidising voluntary agencies. When the blind worker is trained he becomes "employable." In March, 1932, there were 3342 blind persons employed in workshops for the blind, 1631 in home-workers' schemes, and 4151 others who were employed elsewhere. In order that the blind may earn a living wage it is, as a rule, necessary to "augment" their earnings, and it is also necessary to organise the sale of the goods they produce. A large number of home workers are

[1] H.M. Stationery Office, 1934, 1s.

piano tuners. In order to ensure a proper standard of efficiency in these an examination has been instituted by the Board of Education, and it is their aim that no one who has not passed it should in future be recognised as a home worker.

While schemes of employment concern a considerable portion of those who become blind in early life, a large majority of the rest are unemployable—77 per cent. of the total on the register. According to their individual circumstances domiciliary assistance is arranged. The Ministry of Health has laid it down that it is an essential part of the duty of the local authority to secure that "reasonable provision" shall be made for these persons, either by their own officers, by voluntary agencies, or by the public assistance committees. The number of "home teachers" whose functions include the teaching of Braille or Moon type and pastime occupation has more than trebled since 1919, being 85 men and 325 women in 1932. It is now a condition of approval that they should obtain the home teaching certificate of the College of Teachers of the Blind within two years of appointment. The actual work of organising these services is generally delegated to voluntary associations, of which there is a great variety, providing for technical training, workshops and home workers' schemes, and a number of home teaching societies, these latter especially for the unemployable blind. The voluntary agencies are for the most part organised in counties and groups of counties. Nearly all have united to form the Union of Counties Associations for the Blind. There are also three important organisations whose work is of a national character—the National Institute for the Blind, the National Library for the Blind, and St. Dunstan's.

MASTOPATHIA AND CHRONIC MASTITIS

FACED by the frequent introduction of new terms for disease, it is well to recall MCFARLAND'S dictum that pathology must remain confused both in theory and in application unless its terminology is so relieved of ambiguity as to be easily understood. No more obvious failure in this respect could be cited than the redundant terminology of mammary lesions, and especially of the condition commonly called chronic mastitis. A vast literature has collected round this disease, but its nature and significance are still matters of controversy. Some regard it as essentially "a productive inflammatory process," and lay stress on its benign character as evidenced by resolution following non-surgical treatment. Others, and they are the majority, are suspicious of its possible outcome, since records point to its frequent association with malignant development. Much of this uncertainty has arisen, not because of its possibly inflammatory nature—a conception now generally discarded—but because, while the term conveys a fairly definite idea to the clinician, it embraces for the pathologist almost any abnormality in the breast which is neither an acute infection nor a true neoplasm, and also covers various types of hyperplasia which indicate excessive but more or less physiological functional activity, as well as later involutional changes. The term is therefore indefinite and unsatisfactory, and many attempts have been made to find a substitute. SEMB'S suggestion, fibro-adenomatosis (simplex or cystica), has not received in this country the attention it deserves; he assumes the underlying identity of the varied types of the disease, glandular, interstitial and cystic, and describes in a logical sequence various degrees of hyperplasia and cyst-formation and their association with other mammary lesions. LENTHAL CHEATLE and CUTLER separate two distinct proliferative conditions, "mazoplasia," described as an exaggeration of physiological activity with epithelial desquamation, spontaneous disappearance at the menopause, and no tendency to neoplasia, and "cystiphorus hyperplasia," a pathological activity with possible outcome in malignant growth.

In a study of mammary enlargement and its symptoms Prof. BECKWITH WHITEHOUSE[1] questions whether these two conditions should be separated, since he has found them very commonly associated in the same organ. He considers that interpretation of microscopical appearances in the breast needs the correlation of cytology with the phase of the menstrual cycle and its possible abnormalities, for while mazoplasia appears to be the result of excessive mammary stimulation by the corpus luteum hormone and subsequent failure of return to the physiological base-line, cystic disease is, in his opinion, the product of similar repeated excessive stimulations, with a breakdown in the balance between secretion and absorption. This may be an explanation, on the functional side, of the progressive cystic enlargement described by SEMB in fibro-adenomatosis cystica. The mammary disturbance is associated, in 70 per cent. of WHITEHOUSE'S cases, with oligomenorrhœa, menstrual headache, and mammary pain with swelling—a syndrome ascribed to excessive formation of luteal hormone as a result of over-stimulation by the anterior lobe of the pituitary. For this disorder, on the analogy of metropathia, he suggests the name "mastopathia" and the final rejection of "chronic mastitis." Rational treatment of this functional upset would seem to be inhibition of the hypophysis. Prof. WHITEHOUSE pays a tribute to CUTLER'S success with Ovarian Residue and records improvement in his own cases with theelin (œstrin), though in both series the numbers so far are very small.

An estimate of the permanent efficacy of therapy along these lines cannot be made until we have news of the eventual outcome in such cases. Meanwhile it appears that mammary hyperplasia still needs elucidation. Though different types of proliferative activity are observed in the same mammary tissue, their identity as phases in a progressive process cannot be assumed and ascribed to the same functional upset. In "chronic mastitis" two types of epithelial proliferation are usually observed: the one an excessive glandular formation of physiological type, or "adenosis," and the other what WHITEHOUSE calls excessive epithelialisation, preferably "epitheliosis," of individual glandular structures. Adenosis is often

[1] Surg., Gyn., and Obst., February, 1934, p. 278.

associated with puberty and adult mammary enlargement and underlies many temporary menopausal swellings; it may result in fibro-adenomatous tumours, but has apparently no connexion with malignant development. Epitheliosis, on the other hand, is a suspected condition, for though many of the cysts formed by proliferation in the glandular structures become atrophic and permanently quiescent, as in the blue-domed type described by BLOODGOOD, we have at present no means of determining in situ the final result of cystic activity. We are in fact faced here by the possibly "precancerous" lesion met with in other tissues. The wide divergence of clinical and pathological findings which have been recorded is evidence that the clinician has inadequate guidance in the treatment of these breast conditions, and suggests that further investigation is needed to throw light on the difficult problems of mammary hyperplasia.

LONG LIFE

COMMON observation suggests that longevity runs in families. Most people could call to mind a family whose members had all reached an age well beyond the Psalmist's allotted span, or (perhaps less readily) one whose members had all died relatively early in life. The drawback to this kind of evidence is that such individual pedigrees may be no more than curiosities; everyday observation tends to put undue emphasis on the extremes and to disregard the normal or average. A family of four, all of whom live to be over 80, is noteworthy and the circumstance is easily remembered, whereas a family of four dying at ages 25, 45, 65, and 80 will attract no corresponding attention. To measure the force of heredity we need a large and unbiased sample of family histories, and so far the material available for study has been somewhat inadequate, being limited to data such as those provided by the peerage, the records of the Society of Friends, and the histories of notable persons and families individually recorded. At first thought it might seem that insurance companies must possess the information required; for an assessment of the weight to be assigned to family history in the prognosis of longevity is of obvious importance to those who sell assurance policies upon lives. A little consideration leads, however, to the conclusion that information provided by the applicant for insurance is useless for the purpose. One flaw is that the age of the parent at death is known in the society's records only if the parent is dead at the time the application for insurance is made. This age is not known if the parent dies after acceptance of the proposed policy-holder. In other words, short-lived parents would be in excess and long-lived parents in defect, since many assurances are effected in early adult life. The second flaw is that "bad" lives do not apply for assurance or on application are rejected, so that those accepted are a physically select group. This explains why workers have fallen back upon the recorded family histories of special social classes. And in these groups a significant, though small, correlation has been found between the length of life of parent and child, and between brother and brother.[1]

In a series of studies on human longevity which is being carried out in the department of biology of the school of hygiene and public health of the Johns Hopkins University, Prof. RAYMOND PEARL (in conjunction with Miss RUTH PEARL) has approached the subject from a somewhat different angle.[2] By the questionnaire method they have acquired case-histories of 1579 persons living at the ages of 90 years and above, and from these have chosen a group of 365 who could give particulars of the age at death of both parents and all four grandparents. For comparison similar data were extracted from family records already in possession of Prof. PEARL'S department. Analysis of this material showed that the average length of life of the six immediate ancestors (taken as a whole) was nearly 16 per cent. greater in the case of the nonagenarians and centenarians than in the comparative group. In addition the average age at death of each one of their six ancestors was substantially higher than that of the corresponding ancestor in the comparative group—a 20–30 per cent. advantage in the case of parents and 10–14 per cent. in the case of grandparents. It was noted, however, that as large a proportion as 13·4 per cent. of the nonagenarian and centenarian group was derived from matings in which *neither* parent was long-lived (long-lived being defined as 70 years or over at death), so that it appears that extremely longevous persons may be bred from short-lived or average ancestry in a small but not negligible proportion. But it may be observed that 45·8 per cent. of the nonagenarians and centenarians, 56·7 per cent. of their fathers, and 53·4 per cent. of their mothers had *both* their parents in the long-lived category, contrasted with 11·9, 37·1, and 30·1 per cent. in the comparative series. A striking difference was also found in the infant mortality-rates; in the long-lived families it was only 59 per 1000, compared with 125 in the life table population of 1901, and 144 in the comparative series. Generally, therefore, these long-lived have kin whose vitality is superior to the average.

To accept these relatively large differences in the duration of life lived by the immediate ancestors, and the sibships, as being due only or mainly to hereditary influences, one must infer that the environmental conditions in the two series of families do not on the average differ significantly—that the long-lived families do not share a common environment superior to that of the comparative series. How far this is true it is impossible to determine. The long-lived persons are, the report points out, not a random sample of longevous persons generally. They are those "whose great age *per se*, or something they did, or that happened to them, caused them to be written about in their local newspapers." A notably long-lived kinship or ancestry might be a factor tending to bring them into the public eye,

[1] See, for example, Mary Beeton and Karl Pearson: Biometrika, 1901, i., 50.
[2] Human Biology, Feb. 6th, 1934, p. 98.

and this would introduce a bias to the series. Such points make it difficult to exclude completely environmental and selective factors, but in general this interesting study adds to the cumulatively convincing evidence in support of hereditary factors in the duration of life. We still lack an adequate measure of the strength of these factors and evidence as to the mechanism of such inheritance.

DINITROPHENOL COMPOUNDS IN OBESITY

DURING the last two years drugs of the nitrophenol group have been widely used in the treatment of obesity, and it may now be opportune to take stock of the experience gained on both sides of the Atlantic. It is clear that the nitrated phenols are powerful and hence potentially dangerous agents, their principal effect being a substantial acceleration of the basal metabolic rate. Three deaths have so far been recorded, for which dinitrophenol was responsible in two and dinitrocresol in the third. The first fatality followed an enormous overdose taken, it seems, intentionally (J. C. GEIGER [1]); the second occurred in a negress who received rather large daily doses of nitrophenol over a period of two weeks [2]; while the third, which formed the subject of a recent coroner's inquest in London, can also be attributed to overdosage for which the patient was responsible. Apart from these deaths there is ample evidence that more or less serious toxic symptoms are not uncommon. Some of this evidence has already been mentioned in these columns,[3] and further instances have more recently been described by J. H. MASSERMAN and H. GOLDSMITH,[4] who observed unpleasant reactions, notably a fall in blood pressure, tachycardia, acidosis, and stupor in 4 out of 18 psychotic patients treated with dinitrophenol. Such drawbacks, however strongly they may argue in favour of caution and rigid control of the sale of the drugs, do not necessarily provide reason for discarding them, for, as I. M. RABINOWITCH and A. F. FOWLER [4] point out, some of the most useful drugs in the pharmacopœia, such as morphia and strychnine, are equally open to abuse. But this argument can be pushed too far. The first care of the physician is to do no harm to his patient. He does not prescribe morphia when aspirin will answer his purpose; neither should he use dinitrophenol until he is satisfied that safer remedies are not available. This elementary principle of therapeutics seems in danger of being overlooked.

It might be expected, with reason, that a drug which stimulates metabolism would be valuable mainly in treating conditions in which metabolism is depressed. The clearest example of such an abnormality is myxœdema, but myxœdema is more than a simple expression of slowed metabolism (DODDS and ROBERTSON,[5] D. M. DUNLOP [6]), and incidentally is *not* generally associated with conspicuous adiposity; so that nitrophenol is useless as a substitute for thyroxine. In the vast majority of cases of obesity the basal metabolic rate lies within normal limits and the excess fat must in theory, and can in practice, be readily dispersed by simple restriction of diet and increased physical activity. It is true that nitrophenol by raising the basal metabolism will increase the total output of heat from the body and will so permit the self-indulgent to eat their cakes while preserving their figures. But this entails habitual use of the drug; and he would be a bold man who, mindful of what was learnt about nitrated aromatic compounds during the war, would ignore the possibility of ultimate damage to the liver.

To revert to more immediate dangers, two facts may be emphasised: the first that, short of periodic measurements of basal metabolism, which are rarely practicable, there is no way of recognising intoxication from overdosage or idiosyncrasy in good time; and the second that, once the metabolic fire has got out of control, the physician is helpless, for as yet he has nothing with which to quench the flames. The question may be fairly stated thus: is it justifiable, in dealing with a condition which almost always responds readily to a little wholesome discipline, to employ instead a drug of unquestioned potency but uncertain toxicity?

[1] Jour. Amer. Med. Assoc., 1933, ci., 1333.
[2] Ibid., Feb. 17th, 1934, p. 523.
[3] THE LANCET, 1933, ii., 1098, 1218.
[4] Canad. Med. Assoc. Jour., February, 1934, p. 128.
[5] THE LANCET, 1933, ii., 1197.
[6] Brit. Med. Jour., March 24th, 1934, p. 523.

ANNOTATIONS

COMPULSORY CONSULTATIONS

THE March number of *St. Bartholomew's Hospital Journal* contains a rumour that the medical consultations held at the hospital are to be abolished. Let them pass, the surgeon might say, for they are only things of yesterday, mere mushroom growths. The old-time physicians rarely saw the patient; they prescribed for him sitting in a coffee house, upon the report of symptoms told them by the apothecary. They were far too individualistic to consult with anyone, least of all with a fellow physician, unless a great nobleman had the gout or a royal personage was about to die. It was far otherwise with the surgeons.

From the earliest times of which there is any record in London the surgeons were the guardians of the public health and were held responsible for the cure of the sick and maimed. They were on duty at the city gates to see that no grossly diseased person was admitted; and as early as Feb. 2nd, 1369, the chief officers of their gild were sworn to take charge of the hurt and wounded and to give true information to the officers of the city about such persons "whether they be in danger of death or not." A few years later when the barbers had become a company they ordained, in what would now be called their standing orders, that "no barber practising the surgical faculty within the liberty of the city should presume to take under his charge any sick person in actual danger of death or of permanent disability from injury without showing him to the master and wardens." Should

he fail to make such a presentation within three days of the patient coming under his care the barber so offending was to pay a penalty of 6*s*. 8*d*. for each day, 5*s*. to go to the chamber at the Gildhall and 1*s*. 8*d*. to the use of the Barbers Company. The master and wardens were to give their advice free, but if the friends of the patient insisted upon making a present "it be evermore divided by the master into even portions under the penalty of a fine of 20*s*." Moreover, "if they do deny or make refusal to go when so called they equally to pay 20*s*."

This presentation of the sick and maimed served two purposes. It ensured that the patient was seen by three surgeons of great experience, and it shielded the practitioner in attendance from any subsequent action for neglect or malpractice. Neither was it very arduous. London was a small place in the sixteenth and seventeenth centuries and every part of the city was within a few minutes' walking distance. The system worked well, for there is no record of the master and wardens abusing their privilege; but there are countless instances of shifty and ignorant practitioners being fined for neglecting their duty. The utility of the regulation was so plain that it was adopted by other towns like Newcastle-upon-Tyne, York, and Bristol, where the barber surgeons had formed themselves into a company. In London it fell into disuse after 1745 when the surgeons separated from the barbers, but the shadow of it remained in the newly formed voluntary hospitals and infirmaries. It was customary, even within living memory, to advise every member of the surgical staff when an operation was to be performed, naming the day and hour. They attended, watched, advised, and, when an emergency occurred, assisted. Even at such well-regulated hospitals as St. Bartholomew's, St. Thomas's, and Guy's the comments of the onlooking surgeons were sometimes caustic, and a reputation could be easily lost or won.

Surgical consultations as they now exist are purely educational. They are a feature of Basle and some other continental clinics where the pathologist discusses with the surgeons concerned the post-mortem findings of the week. They have long been a feature at St. Bartholomew's Hospital, and in a modified form they are in use at the Peter Bent Brigham Hospital at Boston, Mass. At St. Bart.'s surgical consultations began at some time between 1850 and 1860, possibly at the instigation of Sir James Paget, who was always solicitous for the improved teaching of medical students. They are still conducted periodically in the manner in which they began, except that they are now held in a special room instead of, as formerly, in the (only) operating theatre. Punctually at half past one on a Thursday afternoon the surgeons and assistant surgeons assemble and with them a crowd of students. A patient is brought in about whose treatment his surgeon has doubts, or who is suffering from a condition which is interesting on account of its rarity or obscurity. The nature of the case is explained in the presence of the patient, who feels thereby honoured above his fellows. Each member of the surgical staff examines and puts such questions as he thinks necessary and the patient is then wheeled back to his ward. Each surgeon in the order of seniority expresses his views and the surgeon in charge of the case sums up. At Boston the method varies somewhat, for it is based on continental lines. Once a week the physicians and surgeons assemble and the amphitheatre is filled with students. The clinical notes of patients who have died are read out; staff and students alike make a diagnosis from the recorded facts. The pathologist then steps forward and records the post-mortem findings. His statements are sometimes surprising but chastening to self-confidence.

AMŒBIC DYSENTERY AND FOOD-HANDLERS

APPENDED to a paper[1] by those responsible for the public health of Chicago is the report of a strong committee appointed to investigate the outbreak of dysentery in that city last year.[2] This committee is convinced from clinical and post-mortem findings that the infection was without question amœbic. Two hotels were concerned, and as soon as the dysentery was reported from city hospitals steps were taken to examine their food-handlers. This investigation disclosed 15 clinical cases and 11 carriers of *Entamœba histolytica*. Since exclusion of carriers from food service had apparently been successful in bringing to an end a similar outbreak in Chicago in 1926–27, it was again brought into effect. But it did not check the new epidemic and a second survey, financed by the hotels in question, showed that the personnel other than food-handlers was widely infected. Accordingly the sanitary equipment of the hotels was investigated. The height of both is too great for all floors to be reached at the pressure of the city's water-supply, and the upper floors have to be served by means of pumps situated in the basement of one of them; they have thus a common feature in their water-supply. Further, they had in common special risks of three kinds. The lay-out of the water and sewerage systems was typical of that of older buildings in Chicago in that there was a possibility of back syphonage from water-closets into water pipes. Moreover, twice within three days in the summer of 1933 heavy rain flooded the basement with diluted sewage, entering an ice-storage room, which it filled to the ceiling, and covering the floor of much of the area where food was handled. Finally there were cross connexions of serious character between water and sewage lines, or between water lines carrying potable water and water potentially subject to contamination. These grave defects were put right as soon as discovered, but up to January of this year there had been over 700 clinical cases of amœbic dysentery distributed over 206 cities, and over 1000 carriers had been recognised in Chicago alone.

The direct issue here has turned out to be one of engineering and plumbing and not of food-handling, for food-handlers were conspicuous victims and not originators of the epidemic. Nevertheless, the committee has rightly raised the question of carriers and food-handling. It holds that no one passing cysts should be allowed to hold that occupation until, seven days after treatment, there have been three negative stool examinations, at intervals of at least one day, and at least four more at intervals of a month. A. Bassler[3] believes that to ensure a parasite-free condition at least three fæcal specimens should be examined three-monthly for a year. Much, however, depends on the method of examination. By a thorough survey of 55 persons in a mental hospital in Sweden, Ruth Svensson and J. F. Linders[4] have compared three methods of diagnosis: at least six smears from formed stools, a single smear from a loose stool, and culture from the latter. They found that, of all infections so discovered, 73 per cent. were detected by the first, 75 by the second, and 94 by the

[1] Jour. Amer. Med. Assoc., Feb. 3rd, 1934, p. 367.
[2] See THE LANCET, Jan. 6th, 1934, p. 46.
[3] Jour. Amer. Med. Assoc., March 10th, 1934, p. 786.
[4] Acta Med. Scand., 1934, lxxxi., 267.

third. In the most conspicuous failure of the first, 13 examinations failed to detect amœbæ, whereas a single examination from a loose stool disclosed them. The Dobell-Laidlaw culture medium was used with added starch and trypaflavine, the Boeck-Debohlav medium disclosing only 61 per cent. of cases. Svensson and Linders lay stress on the observation that the ease with which infection can be demonstrated depends on the tendency to encyst, and that for *E. histolytica* at least three factors govern this—the host, the food of the protozoon, and concomitant bacterial flora. It may differ greatly again in different groups of persons.

It is clear that the tracking down of all carriers among food-handlers is no easy matter, and that there is considerable room for improvement in technique.

TREATMENT OF LEPROSY TO-DAY

In a review[1] of the treatment of leprosy Dr. Ernest Muir points out that, as no specific remedy is yet available, each writer is guided by his own experience and preference, with the result that the number of methods employed is very large. They range from autogenous and stock vaccines and other protein substances, through the various chaulmoogra compounds, iodides, heavy metals, and a wide variety of irritant drugs, to cauterisation and electrotherapy. Spontaneous recovery is not unknown, and severe infections such as kala-azar and pneumonia have been known to produce surprising improvement, presumably through their general shock effect. Dr. Muir declares that the best results are obtained by raising the patient's general health and resistance to the highest possible level and giving the maximum amount of the most effective special treatment consistent with maintaining the general health. He regards it as important to have a trustworthy means of estimating the patient's resistance. It is, he thinks, a mistake to press the special treatment until a general reaction is produced. The appearance and feeling of the patient are useful, but a patient whose general health is good might still suffer from a lepra reaction. The erythrocyte sedimentation test is invaluable; anything which accelerates sedimentation lowers the resistance to leprosy. When sedimentation is fast it is necessary to proceed with caution and build up the general health; when it is slow the special treatment may be pressed with confidence. Complicating diseases such as malaria, dysentery, venereal disease, pyorrhœa, and other infections and infestations should be corrected as far as possible. To move the patient to a cooler climate is sometimes useful, and a well-balanced diet is essential. The patient should have a regulated daily time-table, with suitable mental and physical occupation to prevent brooding and depression. Physical training should be progressive and include special exercises to correct trophic pareses and deformities.

When the time has come to initiate special treatment, Dr. Muir is insistent on caution, for almost any effective remedy has a depressing effect. The first dose must be tentative, the second should be given only after the negative phase of the first has passed off, and the dosage is gradually raised until the limit of tolerance is reached. This limit may be extended by use. Potassium iodide is considered by most workers too dangerous for general use; the oils appear to give the best results, and of these chaulmoogra or hydnocarpus holds first place. Sodium hydnocarpate or alepol, although less effective than the oil and the esters, has the advantage of being compact and easily preserved. The best method of administration seems to be intradermal infiltration. Oil made from ripe fresh seeds causes little irritation, but, owing to its viscosity, it does not penetrate the intercellular spaces as readily as the esters; this difficulty may, it seems, be overcome if it is heated on a water-bath to 55° C. Oil is much cheaper than the esters and a uniform quality can be more easily secured. The difference in efficacy between the two is not great. The greatest difficulty in treatment is of course the length of time required—three to five years on an average. Good results are impossible without the intelligent and willing coöperation of the patient, and even then the patient should report at frequent intervals for a number of years.

[1] Internat. Jour. Leprosy, 1933, i., 407.

CUTANEOUS MOLES

Pigmented moles, or melanomata of the skin, are equally common in the two sexes and very widely distributed. Indeed, there are very few people who cannot show a few small flat brown or black spots somewhere on their bodies, and there is seldom any objection to their appearance. Removal is sometimes demanded, nevertheless, for cosmetic reasons, and provided the lesions are not counted in scores or hundreds it may well be practicable. When undertaken, however, it must be drastic; there must be no tentative applications of caustics, radium, or X rays. The best weapon of attack upon the pin-point to the pea-sized lesion, whether hairy or not, is almost certainly the electrolytic needle. It is very doubtful indeed if the more modern diathermy point offers any advantages over this older method, and in unskilled hands it is liable to cause deep burns and scars.

From the strictly medical standpoint pigmented moles have a more serious importance in view of their occasional (fortunately very rare) tendency to undergo malignant degeneration with metastasis. T. Butterworth and J. V. Clauder,[1] from a review of 500 published cases, are able to give some account of the circumstances under which this degeneration takes place. In 10 of 50 cases of their own it appeared that trauma had a part in causing the change, and to put the proportion of traumatic cases at 20 per cent. is not excessive in the light of observations by others whom they quote. In practice we may say that the slightest change in the appearance of a pigmented mole, whether flat, raised, nodular, or hairy, papillomatous or verrucose, should indicate removal without delay, and by the diathermic method for preference. Probably the most convenient applicator of this "cold cautery" is the snare, which resembles in size and shape that used for removing polypi from the nose. In the frankly malignant cases, it is suggested, a margin of healthy tissue, 3 cm. wide, should be removed at the same time, and this seems advisable even where malignancy is doubtful. The excision should be carried deep enough to include the fascia covering the muscles. Butterworth and Clauder recommend that deep X ray therapy should follow, but do not say whether the diathermy wound should be sutured or not. There should be no objection to an attempt at suture if the wound is free from sepsis at the time of the operation, and not too wide for the edges to come together without plastic procedures which would open fascial planes and increase the risk of spread. The subsequent irradiation, it is proposed, should include the area of lymphatic drainage and the lymph glands associated, and thus far there would

[1] Jour. Amer. Med. Assoc., March 10th, 1934, p. 739.

probably be complete agreement; but most authorities would be inclined to criticise Butterworth and Clauder's view that the dissection and removal of regional glands is of doubtful value. In the disseminated case such a measure would of course be useless, but in an early case or one of doubtful malignancy most surgeons would advise it. One point cannot be stressed too strongly: the scalpel should never be used to remove the tumour. Furthermore, X rays should not be applied until after its removal, since generalisation, with melanin in the urine, has been observed to follow rapidly in more than one case.

The prognosis is worse perhaps in cases of cancerous mole than in any other form of malignant disease, and it is of vital importance to deal with them in their very early stages. By way of prevention it may be said that any pigmented mole which is situated in an area liable to constant slight trauma or irritation should be removed—e.g., on the foot where covered by the shoe, under a truss, on the face when a razor may damage it daily, and under corsets or braces. A mole that is changing its appearance, colour, or size should be removed by diathermy, and the dissection of regional glands should be considered. Caustics must never be used, and even electrolysis is permissible only for such small lesions as can be wholly destroyed at one sitting.

INOCULATION OF LIVING SPIROCHÆTES IN SYPHILIS

THE success achieved in most of the stages of syphilis by the chemotherapeutic methods at present in vogue has overshadowed the possibilities of specific immunisation. A practical obstacle to vaccine treatment has been the difficulty of cultivating the spirochæte in adequate purity and profusion, but this, it is stated, has been overcome by Hilgermann, who has also found means of reducing the pathogenicity of the living organisms. For some considerable time the dermatological and neurological departments of the University of Debrecen in Hungary have had supplies of an "avirulent" living vaccine, and Prof. E. Neuber [1] is able to report on its clinical use. It has not, for obvious reasons, been injected into uninfected subjects; nor is any mention made of its trial upon animals. Of the 215 syphilitic patients treated 42 received vaccine alone for six weeks, followed by bismuth and arsenical combinations. In the other 173 cases the vaccine and chemotherapy were combined from the first; on the average three or four injections of material, in quantity decreasing from 1·0 to 0·1 c.cm., were given, for the most part subcutaneously. Local reactions resembling those produced by injections of tuberculin were common, especially after the earlier and larger injections, and in 62 cases there was a general reaction, with fever, headache, and malaise. The Wassermann reactions became somewhat more pronounced under vaccine treatment, and it was noted that a series of cases treated in the ordinary way—i.e., without vaccines—attained a negative serum more rapidly than those subjected to the combined injections. In the 42 cases treated with vaccines alone (three injections with a fortnight's interval between each) the clinical manifestations were sometimes improved and the Wassermann reaction remained strongly positive, as was anticipated. The clinical improvement was most conspicuous in cases of gummata in the third stage, whether these were ulcerating or still closed; there seems to have been no objective improvement in cases of roseolar or early maculopapular eruption, although improvement was observed in some cases of condylomata, and adenitis was not influenced to any degree. The most interesting observation was that all the cases treated with vaccine responded thereafter in a remarkable manner to injections of salvarsan or its derivatives, whether they had previously been refractory or not. This leads Neuber to hope that the method may be a useful adjuvant to chemotherapy.

[1] Dermat. Woch., Feb. 24th, 1934, p. 229.

JOHN HEYSHAM AND HIS BILLS OF MORTALITY

STIMULATED by Mr. Norman Maclaren, Carlisle has been celebrating the centenary of the death of John Heysham, one of its most distinguished citizens. A special service was held in the cathedral and the Mayor presided at a meeting when Dr. C. W. Graham delivered an oration on Heysham's life and Mr. W. B. Elderton, president of the Institute of Actuaries, spoke of his world-famous tables of mortality.

John Heysham was born at Lancaster on Nov. 22nd, 1753, and went to the village school at Yealand, near Burton, kept by the Quaker brothers Jenkinson. On leaving school he became "doctor's lad" to Mr. Parkinson, surgeon of Burton, and during his apprenticeship pursued the study of birds, which drove him to become expert in the practice of the bow and arrow. His pupilage over he rode on horseback the 170 miles to Edinburgh, where he graduated in June, 1777, with a thesis on hydrophobia (of which he was destined never to see a case in his 50 years' practice). He then sailed from Leith to Rotterdam for a medical tour of Holland, on returning from which he settled in Carlisle, taking lodgings in St. Cuthbert's-lane, where he lived until his death on March 23rd, 1834. Carlisle was at that time beset with itinerant quacks of all descriptions, and Heysham, well equipped though he was with the medical principles of his time, had a struggle to establish himself as the foremost practitioner in the city, and it seems that his annual income never exceeded £400. His commanding appearance, possibly too the conspicuous brightness of his dress, soon served to make him a well-known figure, and his industry was enhanced by excellent health, for he did not have a single day's illness during his life of 82 years, and this in spite of a well-earned reputation as an epicure. Quite early in his career his thoughtfulness for the needs of his poorer patients led him to apply to the Dean and Chapter for a room above the Abbey Gate in which was founded in 1782 the Carlisle Dispensary, which moved later into the Tithebarn, Heads-lane, and in 1857 to its present site in Chapel-street. This record would have secured him affectionate memory among his fellow citizens, but it was a remarkable excursion into medical statistics that gained for him a wider fame. A few months after settling in Carlisle he meditated a census of the inhabitants and the framing of bills of mortality. He first made sure of the number of the population of Carlisle by a method that in point of accuracy almost amounted to a personal registration of each individual family. This exacting work went on until 1787, when his courtship of the daughter of a rich tanner diverted his attention in other directions. His achievement may be stated in Mr. Elderton's careful words: "He counted the houses and inhabitants, tabulated his results, counted the deaths and set out the causes of death, age by age, person by person, recorded influences likely to affect his statistics, and then took a second census similar to the first. . . . In this and similar tedious work," he added, "lie the roots

of all discoveries, the proof or disproof of any scientific theory, the test of every social remedy—the measure of all improvement." Heysham's work might have remained unnoticed had it not been for a letter dated Sept. 12th, 1812, written from the Sun Life Assurance office in London by its actuary, Mr. Joshua Milne. "Being engaged," he wrote, "in enquiries relative to Human Mortality, and having met with your valuable Observations thereon that were published at Carlisle in 1797, I have constructed a Table of Mortality from them, whereby it appears that the inhabitants of your city surpass in longevity those of any other place (so far as I am informed) for which a similar table has been constructed." This led to a correspondence between the two men, given at length in an appendix to the "Life of John Heysham," by Dr. Henry Lonsdale (Longmans, 1870). Milne finished his work on the Carlisle statistics in 1815 and his tables were still used for annuity valuations in 1875 and even later. They were adopted by other leading assurance companies as the most trustworthy data, superseding the official system then current, and being accepted both in this country and abroad.

It was fitting then that the gathering at Carlisle should have been attended by actuaries and representatives of many life offices. The occasion was utilised to support an appeal fund for renovating the dispensary which Heysham founded. This year too will see the opening of the park in the Raffles area of Carlisle provided by a sum of money left in trust to the city by Heysham himself which has been allowed to accumulate.

A CHEST DIAGNOSTIC SURVEY

AMONGST the various schemes for dealing with the unemployed in New York is one which has a wider significance for civic health than the immediate relief of distress. Dr. John L. Rice, the new health commissioner for the city, records an intensive X ray study of unemployed and their families in the form of a chest diagnostic survey, made possible by a grant from the State Temporary Relief Administration. For this purpose the paper roll film which only costs about one third of the celluloid film has been used. Surveys of the first two sections of the city, Central Harlem and Red Hook, made in 1933 have now been published. A third survey in the West Side section is being undertaken under the direction of Dr. Margaret Barnard who has been closely associated with these X ray studies.[1] Some 20,000 persons have been examined, among whom 512 cases of tuberculosis have been found. Hitherto only 15,727 registered cases were known in the city as a whole. Dr. Rice estimates that if the ratio of cases discovered amongst the unemployed of the Harlem and Red Hook sections prevails in New York City as a whole, the cases should total 180,000. Another surprising fact has been the number of positive cases amongst the white population. In the Harlem district the white women led all others in the proportion of pulmonary tuberculosis. In the Red Hook district, although it is predominently white, the group study showed about 54 per cent. more tuberculosis than in the overwhelmingly coloured Harlem district. These studies suggest that in the unemployed population tuberculosis is four and a quarter times commoner in white than in coloured persons, a surprising and unexpected result. The cases discovered have been placed under treatment.

Use of the paper film has not only lowered the cost of this survey to an economic level, it has enabled the physician to take skiagrams of more than 500 persons a day. Another advantage claimed is the ease and convenience with which the pictures can be read and interpreted, together with an attainment of uniformity in quality. Each picture bears on its face full data regarding the subject—name, address, sex, weight, height—so that time in record making is saved. The diagnosis also may be added to the film, thereby making a complete record of each case. Each 20-ft. roll film contains 100 pictures. The preliminary report issued by Dr. Rice gives no detailed analysis of the X ray findings so that it is not possible at the moment to estimate the value of the paper as against the celluloid film in differentiating between active and inactive, early and obsolete lesions, but the figures are sufficiently impressive to warrant a careful comparison of the two kinds of film in the same patient over a large series.

[1] THE LANCET, 1932, i., 930 and ii., 247.

ILLICIT USE OF NARCOTICS

IN the last report of the advisory committee on the traffic in dangerous drugs to the Council of the League of Nations attention was called to a practice which is becoming prevalent in the Far East of smoking heroin pills. An analysis of these pills made by Prof. E. Knaffl-Lenz, of Vienna, showed that they contain caffeine as well as heroin and sometimes also strychnine or quinine. It appears that at least one-third of the heroin content would pass over to the consumer in the smoke and is capable of producing its physiological effects.

The report of a subcommittee on seizures of illicit drugs contains interesting information regarding contraband traffic in the United States, whence more seizures have been returned than in any other single country. The heaviest arrivals of raw opium were on the Atlantic coast, mostly from Italian ports but of Turkish origin. On the other hand, "prepared" opium reached the States on the Pacific coast by ships from the Far East en route from Hawaii. Illicit morphine entered the States by various routes—e.g., from Japan and China on the Pacific coast, from French ports on the Atlantic sea-board, and from Germany through Central American countries. It is reported that "all the circumstances point to a continuance of illicit traffic in morphine from Western Europe to the United States on much the same scale as for several years past, with a development of new methods of concealment and transportation." Appreciation is expressed at the valuable coöperation of enforcement officers in the United Kingdom, Canada, Egypt, France, Germany, and the Netherlands in tracking and exposing the agencies employed in this illicit commerce. Although the position is certainly better than it was a few years ago yet "it is by no means safe to conclude that illicit import is decreasing."

THE death is reported from South Africa of Dr. Charles Porter, for many years medical officer of health for Johannesburg.

AN election will take place in July next for members of the Council of the Royal College of Surgeons of England. There are four vacancies, and the following Fellows are standing for election:—Ernest William Hey Groves, George Grey Turner, Hugh Lett, C.B.E., Alfred William Sheen, C.B.E., Duncan Campbell Lloyd Fitzwilliams, C.M.G., Gwynne Evan Owen Williams, Ernest Cranmer Hughes, O.B.E., and William Girling Ball. Of these candidates the first three are retiring from the Council in rotation and offer themselves for re-election.

PROGNOSIS

A Series of Signed Articles contributed by invitation

I.—PROGNOSIS IN GALL-BLADDER DISEASE

To the patient suffering from gall-bladder disease, especially that form of it which is associated with recurrent attacks of severe pain, the practical problem of relief depends on the likelihood of improvement or cure under medical measures or the dreaded necessity for operative treatment.

Does inflammatory disease of the gall-bladder ever clear up completely? Does it often pass into long periods of quiescence? If gall-stones have formed may they, under treatment, dissolve or be passed by the bowel? Is the patient's general health likely to suffer from the presence of a diseased gall-bladder, and is any risk to life run by leaving a diseased gall-bladder in situ? Does surgical treatment involve much risk to life? If survived, will the operation relieve all the symptoms? What chance is there of the trouble recurring after operation? Does removal of the gall-bladder per se give rise to any disagreeable or disabling symptoms? Does the presence of a stone or stones in the common bile-duct make the operative risk and the future prospect grave? What is the outlook from operation in the patient who is deeply jaundiced?

These and other questions are being raised daily in practice, and in this communication I will endeavour to answer them.

Might I first emphasise the difficulty in some cases of being sure of the diagnosis and thus of assessing the value of various forms of conservative treatment? I have on more than one occasion, whilst operating for another upper abdominal lesion, exposed a perfectly normal gall-bladder, the known disease in which was said to have been kept in abeyance for years by careful medical treatment. It is inevitable, therefore, that in any series of cases treated on medical lines, we will have a number in which the diagnosis was sufficiently in doubt as to make accurate statistical record impossible. On the other hand, we have a sufficiency of cases in which the diagnosis was clear, and in which medical treatment was employed, to give an approximately accurate estimate of prognosis.

CHANCES OF SUCCESS WITH MEDICAL MEASURES

Have we any reason to doubt that inflammation in the gall-bladder will clear up completely in a certain number of cases? We know that cholecystitis is frequently a chronic and indolent disease; that the causal organism is embedded in the gall-bladder wall and is killed or dislodged with difficulty. We also know that the common association with gall-stones and the intermittent obstruction of the cystic duct which is liable to take place aggravates and perpetuates the cholecystitis. None the less it is true that in a certain number of cases of indubitable cholecystitis, symptoms have disappeared for long periods of years after medical treatment and a lasting symptomatic cure has been effected.

If we have diagnosed the presence of gall-stones, either from typical biliary colic or from X ray demonstration, what chance is there of cure by medical treatment? It may be said at once that no known drug or diet will cause the solution of gall-stones. Can we induce the passage of the stones by way of the ducts and bowel? There is no question that sometimes after the administration of generous doses of olive oil a number of small stones may pass, and this form of treatment is well worth a trial, provided we do not know that there is a stone present the size of which makes passage down the ducts impossible. Experience points to the percentage of cases in which such treatment can be followed by lasting success being extremely small—in the region of 5 per cent.

We have obtained abundant evidence in the past few years of the sinister consequences of untreated gall-bladder infection. Firstly, a stone may lodge in the common bile-duct and give rise to the disabling, and sometimes dangerous, symptoms which follow obstruction of the duct. A suppurative obstructive cholecystitis may be followed by a subphrenic abscess or a pylephlebitis, or a large stone ulcerating through into the intestine may cause acute intestinal obstruction. A pancreatitis, either of the slow sclerosing variety or of the dangerous acute hæmorrhagic type, may develop. Toxic changes in the heart muscle, in the fascial planes, in joints and in kidneys, resulting from absorption of organisms and their toxins from the chronic infective focus in the gall-bladder, are now known to be not infrequent sequelæ of cholecystitis.

Apart then from the dangerous complication where life is in jeopardy, an indolent gall-bladder infection may play a definite and important rôle in bringing about those degenerative changes which, coming on in late middle life, precipitate the patient into a premature old age.

FACTORS DIMINISHING OPERATIVE RISKS

What is the immediate risk attached to operations on the biliary passages? It is obvious that the answer to this question depends on several factors—viz., the care taken in pre-operative preparation, the skill and experience of the surgeon, and the quality of the nursing in the post-operative period. Many patients with biliary disease are bad subjects for operation. They are often very stout and breathless on exertion, and in some cases are poisoned and jaundiced.

The immediate prognosis will be greatly improved if an appropriate pre-operative régime be instituted. If the patient is very obese a delay of three months, during which weight is reduced on a suitable diet with regulated exercise, will facilitate the operative manipulations, and, by ensuring well-maintained cardiac action, will lessen the risk of post-operative thrombosis and embolism. Since adopting a period of pre-operative dieting and physical training in stout, flabby subjects, I have found my mortality-rate in biliary surgery has been reduced to half its previous level. An adequate pre-operative supply of fluid and sugar is another safeguard, especially in cases in which an infected and obstructed common bile-duct has led to loss of weight and impairment of hepatic efficiency.

In uncomplicated cases of gall-bladder disease in which operation has been undertaken on account of recurring colic or chronic dyspepsia, the risk to life from removal of the gall-bladder should not be more than 2 per cent. Evacuation and drainage of the gall-bladder in such cases should bear an even lower mortality; but it is not advised because a diseased organ is left behind, gall-stones recur in approximately 10 per cent. of cases, biliary dyspepsia may persist, and, in some cases, carcinoma of the gall-bladder develops.

Emergency operations.—In cases of acute obstructive cholecystitis where the condition does not yield to expectant and medical measures, operative treatment of an emergency nature must be undertaken. This should consist merely in an exposure, opening and evacuation of the gall-bladder, followed by drainage. In elderly subjects with a tendency to chest complication this operation is by no means free from risk. A preliminary narcotic and local anæsthesia will permit of adequate access and is well tolerated. Where the gall-bladder is partly gangrenous *B. welchii* is usually found. In such cases the abdominal wound should be left open and packed and anti-welchii serum—40 c.cm.—given at once. After such emergency operations recovery may be complete and lasting. My experience has been, however, that in 50 per cent. of such cases symptoms recur, often with the formation of further stones, and in two of my cases with the development of carcinoma of the gall-bladder. Owing to this tendency to persistence of some of the symptoms, to the recurrence of stones, and to the development of malignancy, the operation of drainage of the gall-bladder has been largely superseded by that of removal.

RESULTS AFTER OPERATION

What chance is there of persistence of symptoms after removal of the gall-bladder? We find, from a follow-up, that the patients are relieved of symptoms in over 70 per cent. of cases. The poor results and the qualified benefit are found, for the most part, in the cases in which the pre-operative symptoms were somewhat atypical and the pathology disclosed at operation was not gross. Flatulence, heartburn, and intolerance of fats are the usual residual symptoms. Occasionally attacks of colic will persist after operation, to the chagrin of both patient and surgeon. Such attacks may mean that a stone in the common bile-duct has been overlooked or merely that the sphincter of Oddi is still subject to spasm. Patience and belladonna are indicated for some months after operation in such cases, and only if jaundice supervenes should further operative interference be considered.

There is a fairly widespread impression that after removal of the gall-bladder a patient never quite regains normal digestion. This is quite erroneous. I have questioned many hundreds of patients on this point and the unanimous verdict is that digestion is as good as ever and better than for many months or years before operation. The only exception is where a functioning gall-bladder, the seat of early disease, has been removed; here for some months vague digestive disturbance results but in course of time gradually disappears.

An analysis of the cases in which, following cholecystectomy, troublesome symptoms have persisted has shown that in the majority the disease in the gall-bladder was mild in degree and without stones, and at operation some hesitation existed as to whether extirpation of the gall-bladder was justifiable. In such cases the diagnosis was probably wrong and the operation of cholecystectomy must bear unwarranted discredit. In some cases a stone in the common bile-duct had been overlooked and little, if any, benefit has resulted. In some such cases the disappointed patient will have no further surgical interference; in most, luckily, the patient consents to a second operation, when the duct is cleared, the patient relieved, and surgery rehabilitated.

The lesson is that the common duct should always be displayed and, if any doubt exists, opened and explored at every operation on the biliary tract.

STONE IN THE COMMON BILE-DUCT

When a diagnosis of stone in the common duct is made, surgical treatment should always be recommended. The possibility of a stone, which has been arrested in the duct, passing on into the duodenum becomes less with every day. Surgical treatment, whilst imperative, should not be precipitate. If intermittent jaundice and fever have punctuated the course of the illness, operation should, if possible, be timed to occur with a waning jaundice and a receding infection. When this can be done the risk of operation does not exceed appreciably that of cholecystectomy. If, on the other hand, the obstruction of the duct is complete, jaundice progressive, the stools devoid of bile, and the patient apathetic and drowsy, operation is demanded without undue delay and the prognosis must be guarded.

In the first case chemical disinfection of the ducts by large doses of hexamine and the "schutztherapie" for the liver—glucose and insulin—may with advantage be carried on for a week or more. In the second case intensive pre-operative therapy over a period of 48 hours by intravenous administration of fluid and glucose, of calcium chloride, and of blood, will lessen the considerable risk of hæmorrhage and of hepatic insufficiency, but will not render safe what must be at all times a dangerous procedure.

If on opening the common duct colourless fluid escapes—white bile—this is an index of severe back pressure on the liver and a bad prognostic feature; it calls for special efforts to promote liver function by fluid, glucose, and by diathermy to raise the temperature of the liver.

In spite of all our efforts the death-rate in the deeply jaundiced patient will remain high, not less than 20 per cent. Consequently, we should see to it that patients presenting symptoms of stone in the common duct are not left until they reach a dangerous condition requiring desperate measures.

CARCINOMA OF THE GALL-BLADDER

When malignant disease of the gall-bladder occurs it is almost invariably as a sequel to gall-stones. The gall-bladder is not a very common site for cancer—I have had to deal with 32 cases among some 800 cases of gall-stones, and in just over 1000 operations on the biliary passages. Frequently it does not declare its presence until, on the one hand by obstructing the neck of the gall-bladder, it gives rise to a palpable mucocele or empyema of that organ, or on the other hand by pressure exerted by invaded lymph glands on the common duct it causes jaundice. Seldom, therefore, can the growth be successfully removed—the only successful cases in my experience are those (two cases) where it was discovered accidentally on opening a gall-bladder removed for gall-stones. In all other cases where removal was attempted early recurrence in the liver has taken place. Practical experience of these cases convinces one more and more of the advisability of removing and not simply draining the diseased gall-bladder.

D. P. D. WILKIE, M.D., F.R.C.S.
Professor of Surgery, University of Edinburgh.

AT the recent annual meeting of Melksham Cottage Hospital it was announced that the hospital is about to receive the legacy of £100,000 bequeathed by the late Mrs. Ludlow-Bruges, who formerly lived in the neighbourhood. Owing to the appreciation of securities the sum mentioned will probably be exceeded. A new wing is to be built with a portion of the money. The year 1933 closed with an adverse balance of £639, and the rating assessment of the hospital has been raised from £10 to £87.

SPECIAL ARTICLES

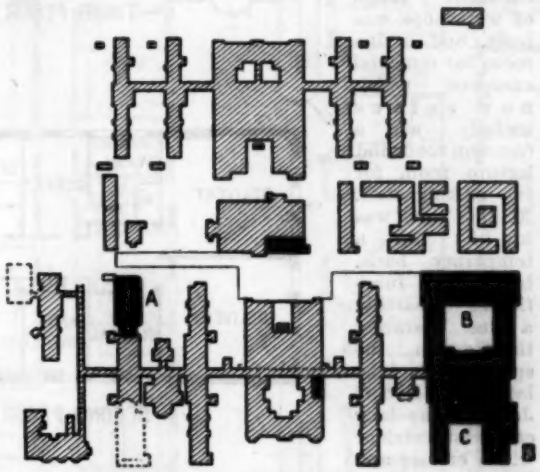
BRITISH POSTGRADUATE MEDICAL SCHOOL

BUILDING is progressing rapidly at Hammersmith Hospital in fulfilment of the scheme which, if all goes well, is to produce by December the framework of a new post-graduate medical school. The foundation-stone was laid last July [1] by Mr. Neville Chamberlain, Chancellor of the Exchequer, in the presence of Sir Austen Chamberlain, chairman of the Governing Body, Lord Athlone, chancellor of the University of London, Sir Hilton Young, Minister of Health, and Mr. E. M. Dence, chairman of the London County Council. The scheme is the joint concern of H.M. Government, the University of London, and the London County Council, and by the courtesy of the Governing Body and the Council we are able to reproduce here the detailed plans of the new buildings.

The foundation of a new medical school in London is in itself an event of some interest. No one living can remember the foundation of any of the 12 undergraduate medical schools in the metropolis. Their growth and development has been dictated by experience of their particular needs, reconciled as far as possible to exigencies of site, finance, and available space. The new post-graduate school is a building de novo, not like the hospital to which it is attached, an adaptation and extension of existing premises; it has been designed and is being carried out solely to embody the ideals of its promoters. What these intentions are may be gathered from the report of the 1930 committee which set out to provide facilities for at least three different classes of students. In the first place, in addition to the permanent teaching staff (professorships in four subjects—medicine, surgery, gynæcology and obstetrics, and pathology—have been advertised), the provision of courses by visiting experts, including acknowledged leaders in medicine and surgery, should, they thought, attract students from the Empire and abroad who at present have no means of taking advantage of practical work in this country. Secondly, they bore in mind the further need for scientific training on the part of those who have qualified at one or other of the British undergraduate medical schools, either in London or elsewhere, with the expression of a hope of bringing these schools into closer interrelation than exists to-day. Thirdly, they were keenly aware of the need of short and highly concentrated refresher courses for practitioners, especially those in the country, to keep them in touch with new developments in medicine and surgery. As one example there are 17,000 practitioners working under the National Health Insurance Acts, and year by year a certain proportion of these should have a chance of taking such courses at a post-graduate school. The plans of the school will be closely scrutinised to see how a committee of great distinction has sought to put these objects into being.

THE CHOICE OF SITE

A domicile for the post-graduate school was a matter which had perplexed and eluded successive committees. The ideal solution of a new hospital specially built and equipped was finally turned down even in times of less financial stress than the present; overtures to one and another of the undergraduate teaching schools, although long entertained, ultimately came to nothing. Four years ago an association with an existing voluntary hospital was becoming definite, when it was seen that the London County Council was itself shortly to be charged with the duty of providing and maintaining public accommodation for the sick poor in London, and the attachment of the school to a public municipal hospital became a new and exciting possibility. The choice gradually



Lay-out of the Hammersmith Hospital, showing existing buildings in grey and additions in black. A is the new hospital wing, with a group of operating theatres. B is the medical school proper. C is the new casualty and out-patient department.

narrowed down to hospitals at Lewisham and Hammersmith (Ducane-road), and finally fell on the latter. The choice of site may be regarded as a happy one, for the hospital is finely situated to the south of a large area of open ground known as Wormwood Scrubs, which is assured in perpetuity. On the west lies the famous prison; and the extensive plot on the east will also remain open, for it has been acquired by the governors of St. Clement Danes grammar school. Ducane-road itself ceased to be a main thoroughfare when Western-avenue was pushed through parallel to it 100 yards away. Between them lies the Central London Railway, on which the new London transport board should be willing to make a stopping place near the entrance gate of the hospital, which would then bring it within a quarter of an hour of Oxford Circus. The grounds of the hospital itself cover 14 acres, and provide ample room for further building.

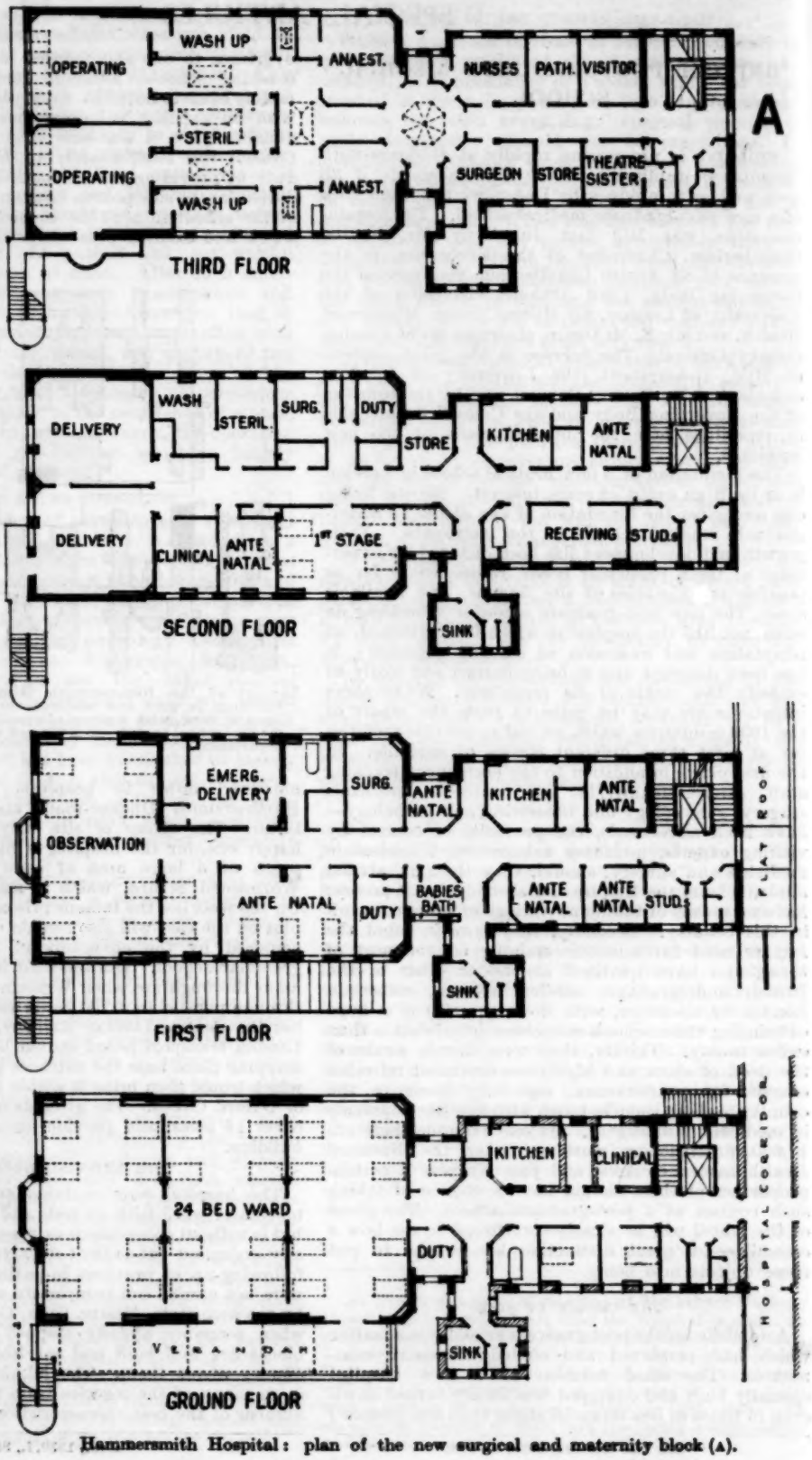
THE EXISTING HOSPITAL

The hospital now contains 400 beds, a modern maternity ward with 16 beds and an antenatal clinic, but is without tuberculosis or venereal departments, or any organised out-patient department except for the following-up of previous in-patients. The buildings were not carried out completely as planned [2] in 1905 by the architects, Messrs. Giles, Gough, and Trollope, when economy already stepped in, but the ward blocks are well built and serviceable with a certain dignity about them. The administrative block, as in so many of the legacies from the poor-law, has a number of the best characteristics of the comfortable

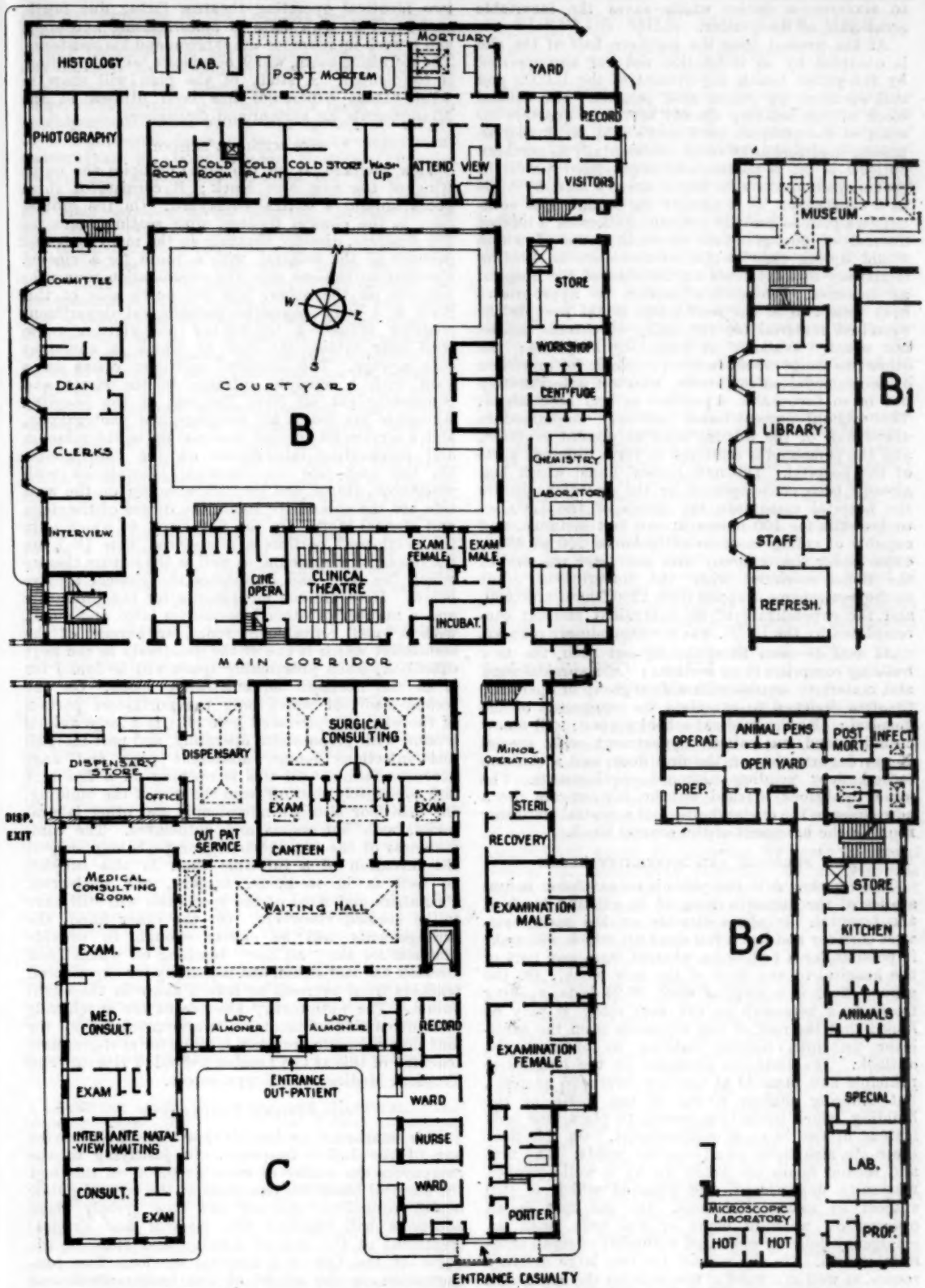
[1] See THE LANCET, 1933, ii., 199.

[2] Ibid., 1930, i., 881.

private house. Important additions were made when it was taken over during the war, and remained from 1918–24 as an orthopædic hospital of the Ministry of Pensions; an excellent range of workshops was built, and a fine room for remedial exercises which now serves usefully as a common room and lecture room for the nursing staff. At this time was built on a temporary basis, but still functioning heartily, a fine operating theatre to the specification of the late Sir Robert Jones. The long east-west corridor which crosses and links up these buildings conveniently will make it readily possible for every ward in the hospital to be used for teaching purposes, and for a case in any of them to be transferred in bed to the clinical theatre of the new medical school. The old stationary beds are already being replaced by wheeled ones—four wheels perhaps would be better than two, and, before it is too late, the committee might consider the ingenious plan adopted at the Clavadel surgical clinic of putting rubber-tired discs on all four legs about a foot from the ground, and a metal strip at corresponding height along all the corridors that the beds are likely



Hammersmith Hospital: plan of the new surgical and maternity block (A).



Hammersmith Hospital: ground-floor plan of the medical school (B) and new out-patient department (C). Parts are also shown of the first floor (B_1) and second floor (B_2) of the medical school.

to traverse—a device which saves the inevitable scratching of the plaster.

At the present time the northern half of the site is occupied by an institution not yet appropriated by the public health department of the L.C.C., and still occupied by infirm aged persons. The central block of this building already serves as quarters for some of the resident staff, and could be further so utilised to almost any extent—incidentally its northern outlook is on a particularly sequestered parcel of ground behind the rifle butts, already used by birds as a sanctuary. It is part of the organisation committee's plan to provide accommodation for a limited number of post-graduate students, some of whom would during their period of residence be holding temporary appointments on the staff of the hospital as internes. When this section is appropriated next year two of the four wings might provide the promised material for the study of chronic disease not usually available at voluntary hospitals; the other two wings would become available for extension of accommodation for nurses, who are unfortunately not in so favourable a position as had been hoped. The original nurses' home can only accommodate about half of the nursing staff at present required, and the personnel is scattered in three different parts of the hospital. The new nurses' home which had already been contemplated by the guardians before the hospital came into the hands of the L.C.C.—to be built for 100 nurses in the first instance, and capable of enlargement so as to house 200 to 250—came under the economy axe, and later was one of the items sacrificed when the Government grant to the new scheme dropped from £250,000 to £100,000, and the expenditure of an equivalent amount contemplated by the L.C.C. was correspondingly reduced.

As will be seen from the lay-out plan, the new building comprises three sections: (A) a surgical ward and maternity section with a dual group of operating theatres designed to complete the equipment of the hospital; (B) the medical school proper; (C) a new casualty and out-patient department with special X ray departments on the first floor, and a skeleton second floor pending ultimate requirements. The minor additions marked on the lay-out are for a new boiler in the engine-house and a central sterilising room in the basement of the central block.

NEW SURGICAL AND MATERNITY BLOCK

This (marked A in the plan) is an extension in four stories of the northern wing of an existing block of the hospital. It abuts directly on the main east-west corridor and has a full-sized lift which will make it possible for a bed to be wheeled from any part of the hospital to any floor of the new block. On the ground floor is a surgical ward of 24 beds, opening freely to a verandah on the west side; it may be hoped that the roof of this verandah is on the cantilever principle, leaving nothing to obstruct the outlook. The beds are arranged on the lengthwise principle now familiar at the new Southend hospital, but differing slightly owing to the width of the building, which made it necessary to place four beds instead of two in each compartment. On this floor there are also three small one-bed wards. The first and second floors are taken up by a well-equipped maternity department, the plan of which is still subject to minor variations. On the first is an observation ward of eight or ten beds, with an emergency delivery room and a number of small ante-natal rooms. On the second are two large delivery rooms, as well as a ward of five beds for the first stage, and other accessory rooms. On the third floor are two identical operating theatres facing due north, each with its own suite of anæsthetising ante-room and a wash-up room for the surgeon and his assistants. The sterilising room, which occupies a central position, is top-lighted. A study of the plan will show to what extent experience has been utilised in the arrangements for system and cleanliness.

THE MEDICAL SCHOOL

This (marked B on the plan) occupies the north wing of the new east block; it consists of three floors around a central courtyard. On the ground floor is the clinical theatre, with seating room for 100 students, directly abutting on the main east-west corridor of the hospital, with a room for a cinema operator on the one side and examination rooms for patients on the other. On the north side of this floor is a very complete pathological department centring around a top-lighted post-mortem room with four tables, attached to which is abundant cold storage. The adjacent mortuary opens on a yard with a separate entrance to the street and completely cut off from the rest of the hospital. Alongside are rooms for histology and photography, and a service lift to take material up to the museum and preparation laboratories on the floor above. On the east side are chemical laboratories with workshops, stores, and centrifuge room; on the west side are the committee room, the offices of the dean and clerical staff. On the first floor, of which only the north-west portion is reproduced here (B_1), are the library and museum, as well as the lecture theatre which lies over and duplicates the clinical theatre below. Here are the laboratories for the professors and a number of other laboratories large and small, with a small refreshment room, an earnest of the restaurant which is one of the desiderata in the next extension, when presumably space will be found for it in the northern administrative block. On the second floor, of which only the north-east portion of the plan is reproduced here (B_2), is a large animal section with preparation, operating, and post-mortem and infectious rooms, abundant pens and cage accommodation. All this is opening on a flat roof and completely shut off from the rest of the building. On this floor also are microscopic and other laboratories, with hot rooms and autoclaves. The completeness of the arrangements for pathology suggest the intention of a full-time chair in this subject, as well as in medicine, surgery, and obstetrics. Pædiatrics and most of the specialties will still have to be studied elsewhere. On the other hand, the arrangements will be elastic enough to provide material for the "ad hoc" teaching on which Lord Dawson has laid stress, and especially for experienced teachers from overseas to take a share in the curriculum. The noteworthy absence of the specifically preventive side of medicine is accounted for by the fact that complete provision is made for post-graduate teaching of this at the London School of Hygiene and Tropical Medicine at Keppel-street.

OUT-PATIENT DEPARTMENT

This (marked C on the plan) is a novel feature for one of the L.C.C. hospitals. In justifying to the ratepayers the outlay of some £100,000 on this and the surgical block the chairman of the central public health committee pointed out how greatly these additions will improve the medical and surgical treatment of the sick of London and enhance the value of the Council's hospital service. The concentration at the school of the best medical and surgical skill available to teach on modern lines will

give opportunities to the Council's medical staff of instruction in the most modern methods of treatment; patients from any of the Council's hospitals can be sent to Hammersmith for the purpose of diagnosis and the specialised treatment available there. The hospital is situated in a rapidly growing neighbourhood—East Acton has sprung up almost in a night—and there is no casualty department nearer than the West London Hospital, 1¼ miles away. The department occupies the whole south wing of the east block, and is situated just opposite the main entrance to the hospital. Nearest to the gate is the entrance for casualties adjoining the porter's lodge; here are two small wards separated by the nurses' room, with ready access to all the other facilities of the department. The entrance for out-patients is in the centre of the block, and opens into a top-lighted waiting hall with sitting room for 300 persons, served by a canteen. Opening out of this hall are two rooms for the lady almoners and suites of consulting and examination rooms, including a theatre for minor operations with recovery room. There is a separate antenatal section with its own entrance. A large new dispensary serves both the main hospital and the out-patients, who have their own entrance and exit. The first floor of this block, which is much reduced in size, contains on the one side a large X ray therapy section, and on the other dental rooms, rooms for heart and lung and gastro-intestinal cases, conveniently separated by the dark room, a fracture room, and various other rooms whose use is likely to be determined by experience. The second floor of this block will remain in skeleton pending ultimate requirements.

We may conclude this account of the buildings themselves with a reminder that the agreement between the London County Council and the Governing Body of the School may be considered to be of a permanent character, although the licence granted to the School for occupation of the new premises is restricted to a term of 999 years. The appointment of the professorial and technical staffs is a matter for agreement between the two bodies. The responsibility for the care of patients will continue to rest with the Council, and while the proper duty of the School is teaching the two functions are in practice inseparable, at least with regard to the more senior posts. The School will depend for its main income on a grant from the University Grants Committee administered through London University (which has two representatives on the Governing Body), but will also receive a payment from the Council in respect of services rendered to the hospital, and, in addition, fees will be charged to students attending courses. The agreement between the two bodies further provides for the setting up of a joint committee, on which the School and the hospitals and medical services committee of the Council will be equally represented, in order to determine all matters of joint concern.

COVENTRY AND WARWICKSHIRE HOSPITAL.—The management of this hospital has decided to acquire the adjoining City Fever Hospital, alter, enlarge, and equip it as an extension. An appeal is therefore being issued for £100,000, which would make it possible to pay off the overdraft of £25,000. The existing facilities have become hopelessly inadequate. The out-patients' department can no longer cope with its rapidly growing attendances, and there is a waiting-list of between 150 and 200, and delicate technical treatments are being given in crowded and unsuitable temporary premises. The extension fund at present stands at about £30,000, and the cost of acquiring the City Hospital will be £65,000.

SURPLUS MILK AND SAFE MILK

A POLICY IN OUTLINE

THE steps the Government proposes to take to increase the consumption of milk and improve the supply were described in the House of Commons[1] on Feb. 22nd. Anxiety, however, has been expressed in the medical journals[2] and elsewhere lest the advantage of greater consumption should be bought at the price of safety—especially the safety of children—and it has been emphasised that the support of the profession will be withheld from schemes which do not include satisfactory arrangements for preventing the transmission of bovine infections.

On March 8th a meeting was held at the London School of Hygiene and Tropical Medicine, with Prof. G. S. Wilson in the chair, and a memorandum on the Government's milk policy was drawn up. We publish here a list of the signatories, followed by passages representing the greater part of their statement.

Dr. J. A. ARKWRIGHT, F.R.S., hon. member of bacteriological staff at the Lister Institute of Preventive Medicine; member of the Medical and Agricultural Research Councils.

Mr. J. C. DRUMMOND, D.Sc., professor of biochemistry in the University of London, at University College.

Prof. J. C. G. LEDINGHAM, M.D., F.R.S., director and chief bacteriologist of the Lister Institute.

Mr. F. C. MINETT, D.Sc., director of the research institute at the Royal Veterinary College.

Prof. H. RAISTRICK, F.R.S., professor of biochemistry in the University of London, at the London School of Hygiene and Tropical Medicine.

Dr. G. S. WILSON, professor of bacteriology as applied to hygiene in the University of London, at the London School of Hygiene.

Mr. N. C. WRIGHT, Ph.D., director of the Hannah Dairy Research Institute.

The Memorandum

The desirability of increasing the consumption of liquid milk is admitted on both economic and public health grounds. Investigations on children have shown conclusively the value of a daily ration of milk in promoting physical growth and development. There is reason to believe that the raising of the per caput consumption of milk from its present value of between one-third and two-fifths of a pint to a higher level would be attended by most beneficial results. A propaganda campaign to achieve this object would probably receive the strong support of the medical and veterinary professions, provided satisfactory assurances were given as to the safety of the milk so supplied.

NECESSITY FOR A SAFE MILK-SUPPLY

Evidence is accumulating rapidly that the raw milk-supply of this country is often heavily infected with micro-organisms capable of producing disease in man. An average of 6·7 per cent., running up in some districts to as much as 20 per cent., of samples of raw market milk are infected with virulent bovine tubercle bacilli. Approximately 20–30 per cent. of raw milk samples can be demonstrated to contain *Brucella abortus* which causes both contagious abortion in cattle and undulant fever in man. It is therefore not surprising that in England and Wales about 2000 deaths every year, mainly in children, occur from tuberculosis of bovine origin, and that at least 4000 fresh cases of this disease are notified annually. The occurrence of undulant fever has only been recognised of late years in this country, and its exact incidence

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[1] THE LANCET, March 3rd, p. 491.

[2] THE LANCET, Feb. 24th, p. 405, and March 10th, p. 526; Brit. Med. Jour., Feb. 24th, p. 339.

is unknown. There are grounds, however, for believing that about 500 cases of active infection with *Brucella abortus*, derived to a considerable extent from milk, occur annually in England and Wales. This estimate, it may be noted, agrees well with the figures of other countries having a similarly infected bovine population.

Besides tuberculosis and undulant fever, numerous milk-borne outbreaks of scarlet fever, septic sore-throat, diphtheria, enteric fever, dysentery, and gastro-enteritis have occurred of late years. We may mention, in particular, two recent outbreaks, one of septic sore-throat at Hove resulting in over 1200 primary cases with 65 deaths, due incidentally to consumption of raw milk coming from an exceptionally well-managed farm, and one of paratyphoid fever at Epping involving 312 persons with 8 deaths.

It is impossible scientifically to escape the implication of these facts—namely, that no raw milk can be guaranteed as safe for human consumption. Milk from tuberculin-tested herds is for all practical purposes free from the risk of conveying tuberculosis, but, as experience both in this country and the United States has shown, it is capable of carrying other infections.

Milk is so liable to contamination, not only from the cow, but also from infected water-supplies used for cleaning utensils, and from human carriers and early cases of disease during its production and distribution, that it must always be considered as potentially dangerous in the raw state.

We do not wish to convey an exaggerated impression of the frequency of milk-borne disease, but we do wish to point out that the potential dangers of raw milk are such as to preclude members of the medical profession who are acquainted with the facts, and who are responsible for the health of those under their care, from recommending it for human consumption.

The logical conclusion to which this argument leads is that all liquid milk should be submitted to some form of adequate heat treatment, preferably low-temperature pasteurisation. There is no doubt that pasteurisation carried out under commercial conditions in properly designed plant efficiently operated can be relied upon to render milk safe. We are of opinion that ordinary raw milk should be pasteurised under official control, and that every step should be taken to ensure that pasteurisation is efficiently performed.

There is reason to believe that if the present Milk Designations Order was amended so as to permit of the pasteurisation of milk from tuberculin-tested herds it would meet with strong support from the medical profession. Hitherto very little progress has been made in the establishment of these herds, partly because the medical profession has no confidence in the safety of Certified and Grade A (T.T.) milk, so far as the risk of conveying diseases other than tuberculosis is concerned. If permissive powers were given to pasteurise milk from tuberculin-tested herds, there would become available a clean safe milk, which we venture to believe would receive very strong support from the medical profession. Experience in the United States may be called upon to justify the truth of this prediction.

The evidence at present available affords no support to the statement still frequently made that pasteurisation seriously diminishes the nutritive value of the milk. The expression of opinion in the Report of the Medical Research Council for the year 1932–1933 amply bears out this conclusion.

There are strong grounds for believing that the adequate pasteurisation of all liquid milk intended for human consumption in this country would abolish the yearly toll of disease and death due to milk-borne infection, and we can see no reason why steps should not be taken to hasten the achievement of this highly desirable result.

OUTLINE OF A MILK POLICY BASED ON SCIENTIFIC PRINCIPLES

The purpose of this memorandum is to offer constructive criticism, and we therefore submit the following proposals outlining a policy which might obtain the support of medical, veterinary, and agricultural interests.

(1) *Stimulation of clean milk production.*—Experience has shown that the production of milk free from dirt and excessive numbers of micro-organisms is possible if a few essentials are adhered to, such as washing of the milker's hands, washing of the cow's udder, and, most important of all, sterilisation of milking utensils. The carrying out of these measures is largely provided for in the Milk and Dairies Order, 1926, and enforcement of this Order would necessarily result in a considerable improvement in the cleanliness of the milk-supply. We would emphasise that dirty milk cannot be made clean by pasteurisation, and that only with milk produced under cleanly conditions is it possible to obtain a satisfactory pasteurised product.

(2) *Permissive powers of compulsory pasteurisation* should be given to towns of 10,000 inhabitants and over. The adequate supervision of pasteurising plants by the local authority should be made obligatory, so as to justify the confidence that the public places in pasteurised milk. Consideration should be given to the possible use of small pasteurising plants by producers in rural districts. All raw milk that cannot be adequately pasteurised should be boiled for use.

(3) *Establishment of a pre-pasteurisation standard of cleanliness.*—It is often urged that pasteurisation diminishes the incentive to produce clean milk. This, we maintain, is unjustifiable. A clean milk is almost as desirable as a safe milk, and the aim for which we must all work is a milk produced under cleanly conditions from healthy animals rendered safe by pasteurisation and distributed in sterilised bottles. A pre-pasteurisation standard of cleanliness, to which all milks intended for pasteurisation must conform, would stimulate enormously the production of clean milk. Such a standard, we believe, is quite possible to set up, and provided it is interpreted liberally in the early stages of its operation, no undue hardship should result.

(4) *Alteration and simplification of the present grading system, with permissive powers of pasteurisation of milk from tuberculin-tested herds.*—We do not propose to suggest new designations at the moment, since they will need a considerable amount of discussion. We do wish, however, to suggest that permissive powers of pasteurisation of milk from tuberculin-tested herds will stimulate enormously the establishment of this type of herd, and will aid the veterinary profession in its campaign against bovine tuberculosis. Pasteurised tuberculin-tested milk will be the cleanest and safest milk on the market; its retail price should not be more than 2*d.* a quart dearer than ordinary pasteurised milk; and it is likely to receive strong recommendation from the medical profession

(5) While in thorough agreement with the desire of the Government to clean up the milking herds of

the country, we feel that nothing short of the *establishment of tuberculin-tested herds* on lines similar in principle to those that have proved so successful in the United States of America is worth serious contemplation. Though clinical inspection and bacteriological sampling of the milk may eliminate a certain number of animals with obvious disease, they can have little ultimate effect on the extent of infection, since animals with clinically detectable disease constitute only a fraction of the total number infected with the tubercle bacillus. They do not accomplish the eradication of tuberculosis, nor do they provide a sufficient guarantee of safety for the milk-supply to justify its increased consumption. We therefore favour a plan, based at first on voluntary coöperation, for the gradual establishment of tuberculin-tested herds, and for the paying of a premium on the milk from such herds whether intended for pasteurisation or not.

(6) We urge that the £750,000 promised for improving the purity of the milk-supply, and of the £500,000 for propaganda purposes, should be devoted to furthering the suggestions laid down in this memorandum rather than on the proposals at present contemplated by the Government.

(7) We further urge that before any definite legislation is introduced, a committee should be appointed consisting of representatives of the producing and distributing interests, and of the Ministries of Health and Agriculture, together with independent scientific authorities, to draw up a plan for the immediate improvement in the cleanliness and safety of the milk-supply of Great Britain. We believe that very striking results might be achieved in a short time at comparatively slight cost if only agreement on fundamental principles was reached. The provision of a clean safe milk-supply is possible only if medical, veterinary, and agricultural interests are united in the support of a plan based on scientific knowledge. The time seems to us to be ripe for the translation of scientific knowledge into current practice.

A Deputation to the Ministers

On March 27th Sir Hilton Young (Minister of Health) and Mr. Walter Elliot, M.B. (Minister of Agriculture), received a deputation introduced by Sir Austen Chamberlain as chairman of the governing body of the London School of Hygiene. The members were Prof. Wilson, Dr. Arkwright, Prof. Ledingham, Dr. Minett, Prof. Raistrick, and Dr. Wright, and their object was to urge the valency of the views set out in their memorandum. In reply the Ministers stated that the points raised were under examination by the Cattle Diseases Committee of the Economic Advisory Council, and the report of the committee and the views of the deputation would receive the careful consideration of the Government. The legislation about to be introduced would be in general terms, and would permit full consideration to be given at a later stage to the matters under discussion.

HOSPITAL COSTS.—Last year the average total cost of each of 2309 in-patients at Worcester Infirmary was £7 10*s.*, as compared with £6 10*s.* in 1932. The average cost per occupied bed was £136 9*s.* 9*d.*, as against £129 18*s.* 10*d.* in the previous year. Each out-patient cost 10*s.* 5½*d.*, a fractional fall.—At the Chelmsford and Essex Hospital last year in-patients (1877) cost £3 5*s.* 7¼*d.* each per week, an increase of 9*s.* 6*d.* per patient; the explanation of the rise was that there were 132 fewer in-patients.—At Croydon General Hospital 2576 in-patients (daily average 116; average stay 16·5 days) cost £6 16*s.* 7*d.* on the average.

HOOKWORM ANÆMIA: ACUTE AND CHRONIC

ACUTE ankylostomiasis is an entity which has been too little studied, and it is useful to have the observations now reported by B. K. Ashford and G. C. and F. K. Payne.[1] The outbreak they describe was in Porto Rico and concerned seven previously healthy persons, of whom six bathed in the sea at a spot where a muddy infective stream was discharging flood water. The whole of those parts of their bodies under their bathing suits became covered with intensely irritating "bites," and acute illness set in with fever, rawness of the throat making swallowing difficult, epigastric pain and vomiting, diarrhœa, intestinal hæmorrhage, and rapidly developing asthenia and pallor. In the most serious case typhoid with hæmorrhage but with delayed agglutination had been diagnosed, but Colonel Ashford was satisfied that he was faced by acute ankylostomiasis, a diagnosis justified by the first appearance of the eggs in the fæces a few days later. Noteworthy is the presence of fever which, it appears, has also been demonstrated as a feature to be expected in acute Mansonian schistosomiasis in Porto Rico. In every case blood, patent or occult, was found in the fæces, and in the most serious of them the loss was so great that the patient's life was only saved by two blood transfusions. The throat symptoms were evidently due to the presence of larvæ there during their well-known passage from skin to intestine. On the digestive symptoms light has been thrown by J. Stewart,[2] whose experience is that heavy nematode infections lessen protein digestion, while from the worms themselves can be extracted a body (he terms it nezyme) which in-vitro experiments show to inhibit the action of pepsin; the effects on intestinal digestion will doubtless be investigated later.

These cases, as well as that of a seventh child who had not bathed but had delved with her hands in the mud bordering the infected stream, were followed by Ashford through daily, and later less frequent, blood examinations for a year; and by the Paynes through examinations of all stools for a month and afterwards on all occasions of anthelmintic treatment, these examinations being so minute as to recover young worms only 1·8 mm. long. Although all but the child bathed for about the same period and appeared to have been about equally peppered with "bites," it is significant that the number of worms recovered varied from 21 to 1439, and from the delving child 7 only. The blood changes were remarkable: a leucocytosis, preponderatingly eosinophilic, reaching its maximum three to four months after infection, the eosinophils in the last case comprising 90 per cent. of all leucocytes. The explanation offered for this striking condition is that it was due to strayed larvæ surviving in numbers in the tissues for that period and then mostly dying, an explanation which though merely inferential at present will have to be in the mental foreground in future work. At all events the fact that such close and skilled fæcal examinations disclosed only 7 worms in one whose hæmoglobin fell to 60 per cent. and erythrocytes to 3,824,000 should give pause to those who hold that 25 intestinal hookworms constitute a negligible load.

As to the cause of the anæmia, the presence and influence of blood loss were unquestionable in these acute cases. But that it wholly explains that of chronic hookworm infection is questioned by C. D.

de Langen.[3] He points out that fæcal blood cannot always be demonstrated, though in general the reaction is such as would have been produced by taking 2 to 3 c.cm. of blood by mouth; and again that the abstraction of one thirty-fifth of a sheep's blood weekly for four years left it in prime condition with a normal blood picture. Nor is increased hæmolysis a sufficient cause, for his experience in this condition is one of lessened fragility of red corpuscles and therefore lessened hæmolysis. The root cause lies in aplasia, and in its production de Langen urges the effects of diet, and in particular implicates the lipoids, cholesterin and the phosphatid lecithin; essentially he uses Miyagawa's theory of autoregulation—namely, that the intravascular death of an erythrocyte provides to the bone-marrow the most important stimulus for the formation of a new one.

The young erythrocyte contains cholesterin which prevents hæmolysis, but as it circulates in the blood it slowly adsorbs lecithin and this, or the higher unsaturated linolenic acid, brings about hæmolysis. There is normally a balance between the two substances, but when adsorption of lecithin reaches a certain level the corpuscle disrupts, and bodies so set free activate the marrow. Thus on a lecithin-rich diet of oats the serum of rabbits may be pink from hæmolysis but the numbers of red corpuscles do not fall; and in a bled rabbit erythrocytes increase, with reticulocytosis, more rapidly on a lecithin-rich diet than in one poor in that substance. This implies that within limits the hæmolysis of erythrocytes within the circulation is the best stimulus to the red marrow to produce more, though, as experiments show, this spurring may be overdone. Moreover in a heavy hookworm infection a considerable area of intestinal epithelium is sucked off, and it appears that it is absorption of lipoids which is first affected by this change.

It is on this basis that de Langen explains the effects of diet in producing hookworm anæmia in Java. It is rife amongst the poorest whose food is frugal with preponderance of carbohydrates, little protein and that vegetable, and fats and lipoids mainly vegetable and of subordinate value. Hæmolysis is thereby lessened, and a daily small loss of blood which would readily be made good by a well-nourished bone-marrow becomes the proverbial last straw. It is, however, noteworthy that, although in malaria hæmolysis occurs within the circulation, in hookworm infection (as has been mentioned) there is less intravascular destruction of red corpuscles than normal, so that their disruption can hardly act directly as a marrow stimulant; nor indeed is their iron stored within the body for the building of new ones. Ashford, too, is sure that in Porto Rico diet is important—that, speaking generally, a diet deficient in protein (in preventive advice he specially mentions animal protein) is a main factor in causing hookworm anæmia, in checking the marrow in its efforts to make good the loss of erythrocytes caused by blood sucking. Dietary defect does not, however, apply to the acute cases he reported which occurred among cultured whites; yet these persons were all still anæmic a year after infection in spite of their economic advantages. But it needs note that none of them had been completely freed from infection even after three to eight treatments with hexylresorcinol and carbon tetrachloride. That such slight infection cannot be disregarded as causing persistence of anæmia the recent report from Syria shows.[4]

In the marrow itself the plastic reaction has its various stages,[5] and at one or more of them the overtaxed marrow evidently ceased to function in the Porto Rican cases. This key position held by the marrow in combating hookworm anæmia has of course long been known; an importance of these investigations is that they throw some further light on the steps of the essential mechanism. This small epidemic is also noteworthy in that infection took place in the sea. It has been known since the opening of the century that the newly hatched hookworm larva is rapidly killed in a salt solution of sea-water strength, so that from fæces deposited in the sea the infection can hardly be carried; but less stress has probably been laid on the observation, known for nearly as long, that infective larvæ have survived in such a solution for a month, so that, as now unhappily demonstrated, a most severe infection can be acquired in the sea when infective larvæ are washed into it and have some such purchase for penetration of the skin as is afforded by a bathing suit.

Ashford's minute investigations were carried out in the face of crippling disability, and the equally exact ones of the Paynes were done with stools often disgustingly offensive from putrefying blood. But their devoted labours have outlined a clinical entity, and their stimulating suggestion as to the effects of strayed larvæ is one which is sure to be further tested. Moreover, their and de Langen's work must weigh heavily against the curiously persistent legend that the gravity of an individual hookworm infection depends solely on the intestinal load, with the victim's body as a passive nonentity.

REFERENCES

1. Puerto Rico Jour. Pub. Health and Trop. Med., 1933, ix., 97.
2. Third Report Univ. Cambridge Inst. Animal Path. for 1932–33, pp. 58 and 77.
3. Proc. Roy. Soc. Med., 1933, xxvi., 763.
4. See THE LANCET, 1932, ii., 588.
5. Med. Research Council Ann. Rep. for 1932–33, p. 16; see THE LANCET, March 10th, 1934, p. 535.

THE SERVICES

ROYAL NAVAL MEDICAL SERVICE

Surg. Lts. (D) to be Surg. Lt.-Comdrs. (D): P. S. Turner, T. G. à C. Emberson, and A. A. Gardner.

The following appointments are notified: Surg. Comdr. W. Gemmell to *Pembroke* for R.N.B.

Surg. Lt.-Comdrs. W. A. Hopkins to *Orion*; S. G. Weldon to *St. Angelo*, and as Naval Health Officer, temp.; and D. A. Newberry to *President* for three months' course.

Surg. Lt. W. D. Gunn to *Victory* and to *London* on recommg.

Surg. Comdr. C. G. Sprague to *Cyclops*.

ROYAL ARMY MEDICAL CORPS

Rex St. John Lyburn to be Lt.

ARMY RESERVE OF OFFICERS

The undermentioned having attained the age limit of liability to recall, ceases to belong to the Res. of Off.: Major P. S. Stewart.

TERRITORIAL ARMY

P. R. Goodfellow (late Cadet Corpl., Clifton Coll. Contgt., Jun. Div., O.T.C.) to be Lt.

INDIAN MEDICAL SERVICE

Majs. N. D. Puri and J. B. Vaidya to be Lt.-Cols.

Capt. E. V. Claydon retires, receiving a gratuity.

Lt.-Col. N. M. Wilson to be Col.

Pritam Varialsingh Karamchandani to be Capt. (on prob.).

ROYAL AIR FORCE

Dental Branch.—Flight Lt. A. P. Atkins is transferred to the Reserve, class D (i).

PANEL AND CONTRACT PRACTICE

The Increase of Canvassing

THERE seems little doubt that the practice of canvassing for patients is on the increase, although it might be hard to ascertain how much of it is due to the difficulty felt by many practitioners to make ends meet, and how much to the lack of ethical training in the curriculum. The General Medical Council has laid down that canvassing is contrary to the public interest and complaints are considered by the Council in this light when brought to their notice. Reference to the index to the Council's minutes will give some idea of its prevalence. It is, however, open to any practitioner who has what he considers sufficient evidence of this practice to lay a complaint before his panel committee. The ethical subcommittee will consider the complaint, and invite the complainant and the doctor against whom he makes the complaint to appear before them to give evidence, upon which they will arrive at a conclusion as to whether the complaint is substantiated or not.

The course to follow in the event of the complaint being substantiated was the subject of debate in the London panel committee at its last meeting. The complaint of canvassing made by Dr. A against Dr. B was found to be proved. It was decided eventually to make representations to the Minister of Health that Dr. B's conduct had been prejudicial to the Service and that he should be removed from the panel. This decision means that the whole case will be tried again de novo by officials of the Ministry when the panel committee will be required to prove that Dr. B did canvass the patients of Dr. A, and both sides are entitled to legal assistance. The case is therefore sub judice, but the facts submitted to the committee may be briefly set out. The practice of Dr. A was originally in the possession of Dr. B. He sold this practice to another practitioner, Dr. C, in October, 1931. Part of the purchase price was paid in cash and a substantial balance was payable by quarterly instalments. Owing to Dr. C borrowing the whole or the bulk of the purchase price, Dr. B has stated that he was not permitted to have any security on the practice. Dr. C defaulted and went bankrupt. The lease of the house which belongs to Dr. B was disclaimed by Dr. C's trustee in bankruptcy, and when the mortgagees sold the practice to a further practitioner Dr. D, the house next door was taken at a lower rent and the practice transferred there. Dr. D in due course sold the practice to Dr. A. This was in September, 1933. On May 9th, 1933, Dr. B returned to his original address to practice, as the usual clause with regard to the restriction of practice was no longer enforceable through the default of Dr. C. Dr. A contended that Dr. B canvassed insured persons on his list to transfer to him. He supported his contention by signed statements from six insured persons. The hearing of this case occupied the committee three days.

This is the first occasion in London that the panel committee has made such representation. There was one previous case of a serious complaint which was tried before the whole committee, counsel being present for both sides conducting the case. But a court of 80 members is too cumbersome, and such cases are now dealt with by the ethical subcommittee. The question naturally arises as to whether it is good policy for the panel committee to act the policeman and conduct a complaint before the Ministry against a practitioner. An amendment was moved that the case should be sent to the medical service subcommittee for investigation, but this was lost by a small majority. The panel committee has no power to call witnesses, and its only penalties are (1) a letter of censure which may be mild or severe; (2) representation to the Ministry for removal from the panel; (3) to send the case to the General Medical Council. The opinion of the minority was that the medical service subcommittee being a statutory judicial body competent to call witnesses and pay their expenses would be better able to present a case to the Ministry than would the panel committee, which would certainly require to employ and pay for legal assistance. The majority however—amongst whom were several who had spent much time on the case in subcommittee—thought the panel committee should have the courage of their convictions, and should not put on other shoulders work they had the power to do themselves.

An Ethical Committee in Search of Truth

The ethical subcommittee of an important panel committee recently had under consideration a complaint made by one practitioner (Dr. A) against another (Dr. B) alleging that he influenced an insured person formerly on his (Dr. A's) list to transfer to him. Dr. A submitted a signed statement from the insured person in question (Miss V) to the following effect:

"In the summer of 1932 I went round to Dr. B's surgery for medical attention for a friend of mine. Among other questions Dr. B asked me who my doctor was. I told him that Dr. A was my doctor. He then asked me whether I liked Dr. A or not. I told him that I liked him as a doctor. He then asked me if I would like to come on his register. I did not really wish to go on his register so I said I would think it over. I went round several times for medicine for my friend, and he asked me again if I had thought it over. My friend told me he was treating her quite well so I let him have the panel cards of my father and myself. Neither of us signed any letter expressing any desire to change our panel doctors."

Dr. B denied the allegation and submitted a signed statement from Miss V stating that he did not influence her in any way to transfer to him. Both practitioners attended before the ethical committee to submit their observations. Miss V also attended with her mother, apparently at the request of both Drs. A and B. On cross-examination Miss V stated that the statement submitted by Dr. A and signed by herself was quite untrue, and she had done Dr. B an injustice. The report continues: As far as could be gathered from a person of Miss V's temperament, a highly neurotic type, what had transpired was as follows:

Miss V was originally on Dr. A's list until the end of 1932. She accompanied a friend who was staying at her home to Dr. B's surgery. This friend, who was highly satisfied with the treatment which she was receiving from Dr. B, eventually persuaded Miss V and other members of her family to transfer to Dr. B's list. Miss V, to use her own words, "turned huffy with Dr. B about a whitlow on my thumb," and went to Dr. A in January last with a view to transferring back to him. She states that the statement which she then signed, and which has been quoted in the foregoing, was written by Dr. A, and read over to her by him. He then asked her to read it, which she did, but contends that she did not really understand its purport. She signed the statement because she was sorry for Dr. A, who had told her that his practice was declining. She was averse to signing it, but Dr. A had pressed her to do so. She gave way because she thought she would be doing him a good turn, and that the matter would not go beyond Dr. A seeing Dr. B.

Having considered Miss V's evidence and the observations of the two practitioners, the committee decided to take no further action.

CORRESPONDENCE

THE CAUSAL FALLACY

To the Editor of THE LANCET

SIR,—It is not easy to be sure whether Dr. Graham Howe merely wishes us to have some exercise in the field of philosophy, or whether he is seeking to help us in our daily work by giving us more easily used concepts than those by which, as he fears, we are now being hampered. If it is only the former it is, of course, great fun; but if, as I suspect, he has intended to show us a path, then I regret to say that I find him an obscure teacher, and I should be glad if he could clarify many passages in his discourse.

At one place, for example, he describes time as an aspect of matter, but before that he had been insisting that it was a fourth dimension of space, which looks as if time was an aspect of space. If time is also an aspect of matter is space one, too? All this seems very confusing. When he is talking about the space-time continuum Dr. Howe seems to imply that doctors have neglected the time factor in their work.

"... the time concept has not yet displaced the causal concept in medical orthodoxy. Whether it be in mind or body, the material of our observation is thus four dimensional and time must be recognised as being quite as important as the three geometrical dimensions in space,"

which is, I think, what every doctor does recognise, though not in such grandiloquent language.

I wonder too whether the notion of the space-time continuum is really helpful outside of mathematical physics; whether indeed in non-mathematical thinking it has any meaning at all; whether the constant repetition of the phrase to which we have all been subjected for some years has not induced in us a feeling that it has meaning, when really it has none when used in word language as opposed to mathematical language; whether it is not one of those pseudo ideas which Herbert Spencer warned us against 50 years ago. We are all familiar with the people who think they are expressing an idea when they talk of inferiority complex, and who are dumb if you ask them what they mean by complex. Further, the idea has little relevance to the subject of Dr. Howe's paper, which, so far as I can follow it, has reference to the contrast between thinking of the cause of a thing on the one hand, and the conditions in which things occur on the other. Let us take another example.

"... the causal concept allowed us to understand nothing whatever about force, and in fact has utterly obscured the whole problem so as to make it practically non-existent."

How a concept which failed to make us understand a problem could annihilate that problem I cannot conceive. Apart from this difficulty, is the first part of the statement true? Surely the concept of force arose from certain effects which suggested the need of a cause. The idea of force would never have arisen at all save for the causal concept. Again:

"... the satisfaction of the physician at his patient's recovery may well feel inclined to assume the generous reward of having been the cause through the skill of his remedies."

Probably these last two quotations are merely careless writing and Dr. Howe could probably say easily enough what he does mean; but philosophy is hard enough to understand when it is written about clearly and carefully, and careless framing of sentences in so important a paper is blameworthy. The sentences chosen by no means exhaust the list of the avoidable obscurities in the article.

But, apart from all this, is the concept of causation really so very damaging as Dr. Howe makes out? He suggests that physicians are constantly seeking first causes. I am sure that they are doing nothing of the kind. They are constantly and properly seeking causes, not a cause, which are sufficient for their purpose. Every physician is enough of a philosopher to be well aware that the first cause is unknowable, that the idea of causation is extremely difficult to understand, but that there are important things the alteration of which will help his patient to get better. Thus he is called to see someone with fever, abdominal pain, rigidity, and a history of vomiting. He opens the abdomen, finds an inflamed appendix, says very properly that this was the cause of the symptoms and knows that its removal will be followed by their relief. It is the merest pedantry to quarrel with him for thinking he has dealt with the essential cause, a thing he most certainly has done; it is of no help to him to think of the matter in terms of endless chains of sequences one of which included a microbe and the other an appendix; and it is certainly not new thought to consider that there had been an alteration of balance between the resistance of the host and the virulence of the microbe. That was old history when I was a medical student.

So much, however, when it comes down to brass tacks, is Dr. Howe dependent on the theory of causation that when he is attacking Sir Maurice Craig on the subject of insomnia he says: "Insomnia, on the other hand, is said to be *caused* (my italics) by pain or worry, or mental restlessness, with or without the existence of some real external agent; of any of these it may be an *effect*, and it is the *antecedent cause*, whatever that may be, which then requires treatment."

Yet elsewhere we are told that "cause is but a phantasy." I am, Sir, yours faithfully,

T. A. ROSS.

Cassel Hospital for Functional Nervous Disorders, Swaylands, Kent, March 29th.

To the Editor of THE LANCET

SIR,—I am comforted in noting that Dr. Graham Howe, though superior to "causes" in his pathology, is not above "effecting" a restoration of balance by treatment. Effects, in Dr. Howe's hands, have good old-fashioned causes covered with a modern coat of paint in the words "dynamic balance." Hypotheses built cautiously from experience surely must not be damned simply because "causally" tainted. Need we be so careful of our metaphysics? I continue, in spite of the mathematicians (and in their company) to be borne along, a 3-dimensional earthly animal, down an obstinately "one-way" time alley, and the compulsion of flesh and blood seems to me (and to them in their more carnal moments) to be a continual stream of causes and effects. I venture to outrage Dr. Howe's feelings by suggesting that the characters of the universe, even in its present highly delectable and 4-dimensional state, are a "brain-wave," and consequently a remote and curious *effect* of certain mammalian prehensile and phonetic developments.

A hundred years ago Schopenhauer wrote:—

"Philosophers . . . gaily philosophised up in the air until at last Hegelian sophistry (Afterweisheit) reached the happy elevation of denying any parentage to our concepts, and asserting that these concepts are the foundation of all reality."

I wish I knew what Dr. Howe means by "mind-body balance."—I am, Sir, yours faithfully,

Oxford March 28th. H. A. ROBERTSON, M.R.C.P.

MONOCYTOSIS AND GRANULOPENIA

To the Editor of THE LANCET

SIR,—I was interested to read Dr. Hartfall's description of a case of monocytosis and granulopenia with an infection of the gums by Vincent's organisms. In the January issue of the *Archives of Internal Medicine* Forkner describes six cases of acute monocytic leukæmia, with the monocytes in the region of 100,000 per c.mm., and the granulocytes almost down to vanishing point. Four out of these six cases had a Vincent's infection of the gums and pharynx. This certainly looks more than coincidence. Forkner does not appear to have attached any importance to the neutropenia; none of the cases was given nucleotide, and they all died.

I am, Sir, yours faithfully,

Hoveden-road, N.W., March 27th. E. HINDEN.

To the Editor of THE LANCET

SIR,—My enjoyment in reading Dr. Hartfall's paper (THE LANCET, March 24th, p. 620) was a little discounted by my introduction to the term "agranulopenia." Hæmatological nomenclature is already much encumbered by redundant terms and nowhere is this more evident than in conditions in which the granular leucocytes of the circulating blood are diminished. In 1922 Werner Schultz described a condition which he called "angina agranulocytica"; Friedemann, recognising that angina was not constantly present in this syndrome, suggested "agranulocytosis." Since that time the following synonyms have appeared: granulocytopenia, granulopenia (Harkins); malignant neutropenia (Schilling); the neutropenic state (Doan); agranulæmia (Brookes); and granulophthisis (Lescher and Hubble).

This confusion is increased by the fact that, prior to 1922, Schilling had used the term "agranulocyte" to describe an immature cell of the granular class in which granules had not yet appeared. Agranulocytosis is thus an ambivalent word meaning, alternatively, an increase of agranulocytes or a decrease of granulocytes. Dr. Hartfall appears to use his term "agranulopenia" as interchangeable with granulopenia. Etymologically it can, surely, only mean a decrease in agranulocytes, unless the double negative—the prefix a- and the suffix -penia—gives the word, by an unwarrantable pleonasmus, the meaning of an increase in granulocytes.

I feel, Sir, that you will agree with me that our knowledge of leucopenic states is unnecessarily obscured by what you, a few years ago, so happily termed, "Hypernomenclaturosis."

I am, Sir, yours faithfully,

Bournemouth, March 27th. RONALD BODLEY SCOTT.

MEDICINE AND THE RIGHT OF SANCTUARY

To the Editor of THE LANCET

SIR,—The letter from Mr. Somerville Hastings last week (p. 709) raises an exceedingly important question, that of the right of sanctuary of the wounded with a doctor in times of civil war. It is a subject worthy of the serious study of the historian with a sense of humanitarian and legal values. The material for such a study must be vast, and it would be necessary to make it not only country by country, but also century by century. Even if it were to be confined to one country and one century, the historian would find enough material to hand for an engrossing survey. In France, with its glowing tradition of chivalry, it is not surprising that professional secrecy for all concerned with the art of healing, nurses as well as doctors, is imposed by law. During the recent rioting in Paris, the wounded among the civilians were cared for in the public hospitals as well as at home. No complete census will ever be made of these casualties, and it is unthinkable that any official would dare to challenge the combined authority of the law and public opinion by coercive measures infringing the obligation of medical secrecy. Public opinion has a very fine tradition as well as instinct behind it in this matter, and one of the most dramatic events in the history of medicine and the right of sanctuary concerns Jean-Dominique Larrey, the heroic surgeon of the Napoleonic wars of whom Napoleon wrote in his will: "C'est l'homme le plus vertueux que j'aie connu." During the revolution of 1830, Larrey, then about 64 years old, found himself busy at the Gros-Caillou Hospital in Paris caring for the wounded. His prestige was such that, as he proceeded to his work, the rioters cleared a passage for him, and the troops concerned with the maintenance of order presented arms as he went by. One evening the rioters swept up to the Gros-Caillou Hospital in search of wounded members of the Royal Guards. Larrey ordered every door to be flung open, and as the rioters surged forward he faced them squarely with: "Que voulez-vous? Mes blessés? Ils sont à moi, allez-vous-en!" And they did.

I am, Sir, yours faithfully,

April 2nd. YOUR PARIS CORRESPONDENT.

To the Editor of THE LANCET

SIR,—The political crisis has affected Austrian practitioners in many ways. All Viennese doctors connected with the Schutzbund (the socialist armed force) are in prison, and doctors attending wounded socialists are liable to be imprisoned unless they notify the police of the names and addresses of the patients.

With regard to the position of Jewish doctors, in August 1932 I found that Jewish practitioners had been excluded from the staff of the Kinderklinik, while all Viennese doctors have to fill in papers giving their nationality and religion, and the dates since which both have been held. Jewish medical men are being removed from their existing hospital appointments in many parts of Austria.

Those of us who have seen the excellent public health services in Vienna—housing schemes, day nurseries, swimming baths, and children's hostels—must especially deplore that the chief promoter of all these measures, Prof. Julius Tandler, is now in prison. He returned from safety in Czechoslovakia to Vienna knowing the fate that was in store for him.

I am, Sir, yours faithfully,

Eastdean, April 2nd. STELLA CHURCHILL.

THE THEORY OF VISION

To the Editor of THE LANCET

SIR,—Though all are agreed that the cones of the retina are the percipient elements, no one has shown how the transparent colourless cones can be directly stimulated by light or form a basis for colour perception. Direct stimulation does not agree with the laws of photo-chemistry. According to Grotthus's law no effect can be produced by light unless it is absorbed. Stimulation of the cones, therefore, must be indirect and all the facts point to the view that it takes place through the photo-chemical decomposition of the visual purple.

I am, Sir, yours faithfully,

F. W. EDRIDGE-GREEN.

Board of Trade, S.W., March 28th.

MENORRHAGIA CURED BY SPLENECTOMY

To the Editor of THE LANCET

SIR,—At the meeting of the North of England Obstetrical and Gynæcological Society reported in your issue of March 24th (p. 632) Mr. Carlton Oldfield described the case of a woman, aged 25, who suffered from menorrhagia for three years, with resulting anæmia, and was cured by splenectomy performed by Lord Moyniham. The case was probably one of essential thrombocytopenic purpura hæmorrhagica, although, it was stated, there had never been a purpuric rash or bleeding from other mucous membranes. The low platelet count and prolonged bleeding time, together with the excellent effect of splenectomy, which was followed by the large increase of platelets and a return of normal bleeding time, are most suggestive. The patient remains in perfect health nine months after the operation and menstruation has become normal.

This case reminds me of one I published in the *Proceedings of the Royal Society of Medicine* (clinical section) eight years ago.

A woman, aged 28, suffered from very severe menorrhagia which necessitated her frequent admission to hospital. In one instance the bleeding had continued for several weeks and her red cells had fallen to just over two million. The thrombocytes were almost absent, the bleeding time 15 minutes, and the capillary resistance test strongly positive. The spleen was not palpable. Her temperature went up to 104° F. Nothing proved of any use except blood transfusion. After her full recovery I asked my colleague, Mr. Rodney Maingot, to perform splenectomy at the Royal Waterloo Hospital, and within a few days the thrombocytes had increased to over a hundred thousand, the bleeding time became normal, and the capillary resistance test negative. As a matter of fact, the bleeding time became normal shortly after the operation. Splenectomy was performed eight years ago and menstruation has been normal ever since, while her general condition is excellent, indeed she now enjoys robust health.

I am not at all surprised to learn that in Mr. Oldfield's case "the bleeding time became normal immediately after operation"; for in two of my own cases of essential purpura hæmorrhagica, in which there had been bleeding from the gums and nose for weeks without treatment availing, the loss of blood ceased within a few minutes of the splenic vessels being tied.

I am, Sir, yours faithfully,

April 2nd. BERNARD MYERS, M.D., F.R.C.P.

DUST FROM TARRED ROADS

To the Editor of THE LANCET

SIR,—I am instructed by my association to draw your attention to the title to Dr. Campbell's note on p. 233 of your issue for Feb. 3rd.

The substance of the note does not lead to the inevitable conclusion that cancer will arise from the action of dust from tarred roads; yet there is a great danger that readers seeing the title, "Note on the experimental production of cancer by dust obtained from tarred roads," will be led to believe, unless they examine the subsequent reading matter critically, that the dust from tarred roads is responsible for cancer in human beings, and this may cause much unnecessary prejudice against roads treated with British tar.—I am, Sir, yours faithfully,

R. MURDIN DRAKE,
For General Manager, The Association of British Chemical Manufacturers.

166, Piccadilly, W., March 23rd.

PARIS

(FROM OUR OWN CORRESPONDENT)

ENTERIC FEVER IN MARSEILLES

ACCORDING to Prof. H. Violle, the mortality from typhoid in Marseilles in 1931 was 15·7 per 100,000 inhabitants, while the corresponding figures for Paris, Berlin and London were 4·8, 0·8, and 0·5 respectively. The notification of the causes of death in Marseilles being notoriously defective, the true state of affairs in the town is assuredly even worse than the official returns suggest. Little wonder, therefore, that the last annual meeting of the Medical Society of Marseilles was devoted to this subject, and that it was discussed on three different dates (Feb. 15th, 21st, and 28th). The heads of Prof. Violle's indictment were several: lack of sewers in parts of the town and its suburbs; chlorination of drinking water in the central area only; pollution of the coast line aggravated by the tideless state of the Mediterranean; and consequent infection of shellfish. Prof. D. Olmer stated that about 98 per cent. of the enteric fever in Marseilles was due to the typhoid bacillus, only 1·4 per cent. being due to paratyphoid B, and 0·2 per cent. to paratyphoid A. According to the same authority, the effect of inoculation against the disease is reflected in the relatively high morbidity and mortality in women, few of whom have enjoyed its benefits. He has not only found shell-fish responsible for an imposing proportion of cases, but has also learnt to regard typhoid of such origin as more serious than typhoid contracted in some other way (mortalities of 21 and 12 per cent. respectively). Shell-fish typhoid has a comparatively short incubation period; there is a preliminary stage of slight gastro-intestinal upset with or without jaundice; diarrhœa, hæmorrhages, and perforation are common; and the various stages of the illness tend to run into one another as if the rhythm were accelerated. Its severity may be attributed either to massive infection or to coincident infection—by *B. coli*, for example. With regard to treatment, Prof. C. Mattei and Dr. Isemein recommended Rodet's specific serum, which they say is always harmless and often effective even in desperate cases. Other speakers discussed the value of bacteriophage and found it doubtful. A more favourable opinion was expressed of the transfusion of the blood of a healthy person recently inoculated against typhoid and paratyphoid fever. With regard to preventive measures, typhoid inoculation by subcutaneous injection emerged from the discussion with commendation, whereas Besredka's method of oral immunisation was dismissed as uncertain, as being effective only for a few weeks, and as giving a false sense of security.

THE PHYSICIAN ATTENDS ON HIMSELF

A correspondent in *Concours Médical* for March 18th seeks advice. A war pensioner suffering from pulmonary disease, he has been in the habit of signing his own prescriptions, and was proceeding blithely in this course when a colleague told him that such autotherapy was against the regulations. The legal adviser to *Concours Médical*, Dr. Boudin, reassures him. It appears that according to a law of 1919 every war pensioner is entitled to choose his own doctor; how then could those who administer this law stultify it by discriminating against the doctor most likely to take and interest in the case? A judgment of the law courts in 1920 also rules that a properly qualified doctor is as free to use dangerous drugs for his own treatment as for that of anyone else. It seems therefore that no formal objection can be raised

to the medical pensioner's prescriptions for himself, even when the chemist's bill is paid by the State. But when it comes to the charging of a fee for the medical care he renders to himself, the matter is somewhat different. The French Ministry of Pensions holds that such charges are not permissible; Dr. Boudin, on the other hand, while admitting that there is something "inelegant" about them, does not believe they are strictly illegal. There is common sense as well as a legal aspect to this problem. A prescription can be scrutinised and analysed; and there are limits to the amount of drugs that even the most receptive patients can accommodate. But medical care, with appropriate advice, is a far less tangible commodity; and the medical pensioner, free to rate the visions of his head upon his bed as consultations worthy of remuneration, might well experience some difficulty in maintaining his normal ethical "elegance" as he attempted to assess the value of abstract thought in terms of hard cash.

MARGARINE IN DISGRACE

A report by Prof. L. Hugounenq to the French Academy of Medicine on Feb. 27th dealt with margarine as a food, its dangers to health, and its inadequacy as a substitute for butter. Many of the failings of margarine are already well known, but there have previously been few indictments of it so sweeping and sustained. Its faults, he said, include a comparative lack of digestibility, a deficiency or lack of vitamins, and the absence of acids which give butter an attractive smell and taste. Butter also contains phosphorus which is not to be found in the materials from which margarine is made. In response to this report the following resolution was adopted: "The Academy, considering that certain margarines provoke digestive troubles in certain persons that these troubles are undoubtedly due to faulty conditions of manufacture and purification, that certain margarine factories elude the supervision and control provided by the law, that margarine is a substitute for butter which does not, however, contain all the elements of natural butter (vitamins and fatty acids) recommends that all undertakings, without distinction, which deal with animal fats intended for food, should be under supervision and inspection and subject to full legal control in the interests of public health."

OBITUARY

DAVID LEES, M.B., Ch.B., F.R.C.S. Edin., D.S.O.

WE regret to record the death of Dr. David Lees, surgeon to the Royal Infirmary, Edinburgh, which occurred on March 25th after an operation, in his fifty-fourth year.

David Lees was born in Tarbolton, the son of Mr. Robert Lees, of Lagg, a veterinary surgeon, and was educated at the Ayr Academy and at the University of Edinburgh. He graduated as M.B., B.Ch. in 1907, and was a distinguished student, becoming later resident house surgeon at the Royal Infirmary and house physician at the Royal Maternity Hospital, Edinburgh. He was for a time assistant medical officer at the Bangour Mental Hospital, and then for four years served in France with various units, being several times mentioned in despatches and obtaining the D.S.O. in 1917. In 1918 he obtained the diploma of F.R.C.S. Edin., and was elected surgeon to the Royal Infirmary, and consulting surgeon for veneral diseases to the Royal Maternity Hospital. Of these diseases he made a particular study, his advice being sought in many directions; he was, for example, delegate of the British Social Hygiene Council to Cyprus and to India during 1926–27, with the responsibility of advising various governments on systematic methods of dealing with venereal disease. He had already written largely and practically on the subject, producing papers on vaccine therapy in gonorrhœa, and writing the article on the Vesiculæ Seminales in the Encyclopædia Medica; and in 1927 his book entitled "Practical Methods in Diagnosis and Treatment of Venereal Diseases" went speedily through two editions. This book brought together in readable form the latest ideas and the most recent technique. Some of the plates should have historic value, as they picture syphilitic rashes of which the present-day student sees little owing to effective therapy. And Lees's wide personal experience enabled him to make useful generalisations about various kinds of therapeutic measures. At the B.M.A. meeting of 1927 he recorded observations on 6000 cases of syphilis treated with bismuth, and recorded his own opinion that, valuable as it was for its ease and safety of administration when organic disease was present, bismuth should always be combined with arsenic, except possibly in pregnancy. Brought in contact in the Edinburgh clinic with a highly floating population Lees was early and strongly impressed with the need to follow up the treatment of venereal disease to a successful conclusion if public health was to be efficiently served. He was prominently associated with the compulsory measures embodied a few years ago in the Edinburgh Corporation Bill, believing that, without some kind of assurance of continuous treatment, many sufferers from venereal diseases would neither be cured themselves nor be prevented from remaining a danger to the community.

Lees was a good teacher, emphatic and picturesque, speaking with conviction of things of which he had personal knowledge, and how valuable his services were at the Edinburgh Infirmary is well set out in the following estimate from a distinguished colleague:—"There are certain people who occupy positions which are peculiar and unique because they have created them themselves. David Lees was such an one. His dynamic personality, combined with his obvious sincerity, enabled him to get things done according to his own well-considered plans. His department could not be thought of apart from himself as it was the expression of his character and his energy. His broad interest in medicine made his opinion on all matters connected with his specialty of peculiar value, and his medical and surgical colleagues availed themselves freely of his ever-ready help. Whilst clear-headed and dogmatic in his views, he was singularly free from all conceit, and a saving sense of humour preserved harmony whenever a clash of opinions threatened discord. His interests were widespread; a keen sportsman he took an active part in the athletic side of university life. As secretary of the Medico-Sociological Club he was the moving spirit in promoting discussions on broad public questions in their relation to medicine. It is, however, as an enthusiastic, helpful, and loyal colleague that he will be missed the most by his medical associates in Edinburgh. He had made such a bold and characteristic niche for himself that it is difficult to see how it can be filled. He has left us a very vivid picture of how a man of character and personality may create for himself and

his specialty a position of undisputed authority and importance."—D. P. D. W.

Another personal friend adds to the picture with these words:—"David Lees had a robust personality; opposition did not damp but rather stimulated him to renewed attempts to carry his point. His arguments were not inspired by a subtle diplomacy but by confidence that logic demanded the acceptance of the conclusions to be drawn from the available evidence. If any were irritated by this attitude, they were forced to respect the man, and his influence in the development of his specialty was indubitable, even though he failed to carry through one project which he had most at heart, the making in Scotland of venereal diseases notifiable. In the pursuits of his leisure David Lees presented the same almost boundless energy. A keen golfer, he was so much interested in the encouragement of golf as a game for children that he often gave up his own sport, when on holiday, to organise competitions for boys and girls. His cheerful good nature will be greatly missed at the northern golfing resorts where he spent his summers. His own son shows a remarkable aptitude for the game."

David Lees leaves a widow and one boy.

SAMUEL LODGE, M.D., B.S. Durh., O.B.E.

THE death occurred on March 19th at his residence in Harrogate of Dr. Samuel Lodge, well known in Bradford and Halifax and outside his immediate circle as a specialist in diseases of the eye and ear. He was 68 years of age.

Samuel Lodge was a native of Bradford, the son of a medical man of the same name, and received his early education at the city Grammar School. He entered St. Thomas's Hospital as a medical student and attended courses at various times at Leeds and at the University of Paris. He graduated as M.B., B.S. Durh. in 1887, and was for a time medical and surgical assistant at the Royal Infirmary, Newcastle-on-Tyne. He shortly afterwards began to specialise in the subjects in which he made his considerable name, was elected surgeon to the eye, ear, throat, and nose department of the Halifax Infirmary, and surgeon to the Bradford Royal Eye and Ear Hospital. During the war he was medical officer to the 6th Battalion of the West Yorkshire Regiment, being already a surgeon-major in the Volunteers, and did excellent organising work, receiving for his services on the Army Medical Boards in Bradford and Leeds the O.B.E. Dr. Lodge's connexion with the Halifax Infirmary extended over nearly a quarter of a century, but he had lived recently in semi-retirement. He leaves a widow and four sons, three of whom are in the medical profession, and one of whom succeeded his father at the Halifax Infirmary. Another son, who died recently, was ophthalmic surgeon to the Leeds Infirmary.

SYDNEY GUY BILLINGTON, M.B., B.S. Lond., F.R.C.S. Edin.

THE death occurred on March 17th of Dr. Sydney Guy Billington, who had undertaken much independent research in the attempt to discover biochemical remedies which might be of value in several conditions—notably, influenza and rheumatism and malignant disease. He received his education at the Birmingham medical school, took the English double qualification in 1910, and in the same year graduated at the University of London as M.B., B.S. He later acquired the diploma of F.R.C.S. Edin. He was a successful student, filled house appointments at the Queen's Hospital, Birmingham, and later became resident pathologist at the General Hospital, Birmingham, while he held the same post for a time at Wolverhampton General Hospital. For the last 17 years he was very interested in promoting the use of "Billington's Antibody," and published, in certain quarters, reports on the use of the remedy purporting to show its value in many conditions, in malignant disease among others. He was unable to obtain the support which he considered his due from members of the medical profession in regard to either his theories or his results; his industry and enthusiasm were undoubted, and certain supporters of his views consider that his work, or some of it, may yet receive more consideration than it did during his lifetime.

MENTAL AFTER-CARE ASSOCIATION

Lord Wakefield of Hythe presided at the annual meeting held on March 20th at the Haberdashers' Hall, when Mr. L. G. Brock, chairman of the Board of Control; Dr. Nathan Raw, Lord Chancellor's visitor in lunacy; Dr. Reginald Worth, chairman of the Association, and Mr. J. M. Oakey, the treasurer, spoke of the activities of a year in which 2865 had been helped. The Association boards out patients in cottage homes for a period of convalescence, arranges residence for them during attendance at clinics, gives them grants of money or relief in kind, gives maintenance while work is being found, obtains employment suitable to their abilities, supplies clothing, tools, &c., necessary for employment, and, generally speaking, acts as a personal friend with sympathy, understanding, guidance, and help. The council reported assistance rendered to many societies and hospitals which had referred difficult cases to them. During the year a large number of old patients had applied for help and advice, an encouraging feature of the work being the way in which those who had once been assisted turned to the Association in their later troubles. Help given at the right time is responsible for averting relapses and consolidating recoveries; in 1933 the Association dealt with 591 "pre-care" patients, the great majority of whom were prevented from becoming patients in a mental hospital. New developments in the Association's work include coöperation with the L.C.C. in the supervision of patients leaving its mental hospitals, and the supply to county and other authorities of social workers. The treasurer described the ratio of administration expenses to revenue as one of the lowest of any benevolent organisation in the country. The secretary of the Association is Miss Vickers, from whom particulars can be obtained at Church House, Dean's Yard, Westminster.

NEWCASTLE ROYAL INFIRMARY: ANNUAL REPORT. The Royal Victoria Infirmary, Newcastle-upon-Tyne, last year admitted 12,842 new in-patients, whose average stay was 15·8 days. This was an increase of 590. There were 110,708 out-patients. With the opening of a special new block of buildings for the treatment of orthopædic cases, and the heightening of two pavilions to add new wards, and thereby replace the two wood-constructed wards erected temporarily during the late war, 54 beds have been added to the bed strength, bringing the present complement of beds in the voluntary side of the hospital up to 645. The new orthopædic building cost £31,000. It is hoped that the additional beds will make a sensible impression upon the waiting-list of nearly 2000. There were 1108 motor traffic cases, of which 416 were admitted, involving an average daily occupation of 18 beds. The total cost was £2413, of which £444 was received from insurance companies. On an average only 30 per cent. of the accounts submitted by the hospital have been paid by the companies.

Since the beginning of this year the Royal Victoria Infirmary has benefited by five bequests of the total value of £4900.

PARLIAMENTARY INTELLIGENCE

NOTES ON CURRENT TOPICS

Easter Adjournment

ON Wednesday, March 28th, the House of Lords adjourned for the Easter recess until Wednesday, April 11th. The Royal Assent was given to a number of Acts, including the Rural Water Supplies Act, the Indian Pay (Temporary Abatements) Act, and the Mining Industry (Welfare Fund) Act.

The House of Commons adjourned on Thursday, March 29th, for the Easter recess until Monday, April 9th.

Bills Advanced

In the House of Lords on March 27th a Bill to deal with betting and lotteries was introduced and read a first time. In the House of Lords on March 28th the South Devon and East Cornwall Hospital, the Plymouth Royal Albert Hospital, and the Devonport and Central Hospital Bills were introduced and read a first time. In the House of Commons on March 28th the Birmingham United Hospital Bill was read a first time.

Poor Law (Scotland) Bill

In the House of Commons on March 27th Mr. SKELTON (Under-Secretary of State for Scotland) moved the second reading of the Poor Law (Scotland) Bill. He said that the Bill was only a step, though an indispensable step, to a full and comprehensive modern poor-law statute. The function of the present Bill was to make amendments of the law, most of which were long overdue. The Bill provided that in the case of an able-bodied unemployed man there should be an opportunity, where it seemed desirable, that proper work should be done in return for relief. It also made it possible for the poor-law authority to provide the means for training and instruction. It dealt with poor-house discipline, questions connected with discharge, and a novel feature with regard to taking to suitable institutions a certain type of aged and infirm persons. Clause 4 of the Bill provided that a local authority should, if required by the Department, provide suitable and separate poor-house accommodation for each or any of such classes of inmate as might be prescribed by regulations made by the Department. At present the Department of Health for Scotland had no powers definitely of stimulating local authorities to proceed with the work of improving the poor-houses. Modern methods and the modern point of view demanded that, where possible, there should be proper segregation in their own interests of the classes of people who composed the different types of those requiring assistance. Clause 9 provided for the removal, under full and proper safeguards, to a suitable hospital or other institution of aged and infirm, or physically incapacitated persons who were unable to devote to themselves, or to obtain from other persons, proper care and attention. The procedure would be that on a certificate by a medical officer application might be made by the relieving authority to the Sheriff, who would have to be satisfied that there was a suitable institution to which the person could go. An order could then be made, which in no case lasted for more than three months, for the removal of the aged or infirm person to a suitable institution. Clause 10 gave a new right to the poor of Scotland—namely, that the first 5*s*. of friendly society sick pay should be disregarded in the assessment of their relief. It also incorporated a provision which the Scottish poor had enjoyed up to now—namely, that the first 7*s*. 6*d*. of National Health Insurance benefit should be disregarded. It was provided that a casual poor person should not be entitled to discharge himself from a poor-house before 9 o'clock in the morning of the second day following admission. It was important that when a vagrant or casual poor person was in an institution the opportunity should be taken to cleanse them and their clothing. That was a public health duty and was beneficial to the casual or vagrant person.

Mr. MILNE said that in 1904 a departmental committee reported on the medical relief of the poor. The report stated that in one poor-house they found an inmate undergoing 12 hours' confinement in a cell that was not provided with a seat. It was absolutely dark and without ventilation or heating. The temperature at the time of the visit of the committee was only a few degrees above freezing-point, and other cells were in much the same condition. If abuses had occurred in the past, what assurances had the House that abuses might not occur in future? Another departmental report concerning, not Scotland, but the poor-law system in England, and dated 1930, stated that in a certain number of casual wards the conditions now existing were infamous and intolerable. Some of the committee had visited wards where two men were locked in a small cell that was built for one person, and kept there in darkness for 12 or 13 hours. The point was that that was possible in England in 1930. An unofficial report from a well-informed source stated that some of the poor-houses in Scotland were most admirable. He made no charge against the administration of the Scottish poor-law authorities, who carried out their difficult duties with zeal, efficiency, and humanity, but they had not always the accommodation necessary for detention, much less for solitary detention. In one place the unofficial report stated that a small public assistance shelter had no bath, and the sleeping accommodation was poor. In another case, in a lodging-house where casuals were sheltered at the public expense, it was reported that "the beds were swarming with vermin . . . crowded together, and the floor was filthy." The first thing to do was to provide suitable accommodation.

Mr. BUCHANAN urged that the power to remove old people was one that was capable of the worst abuses and should be removed from the Bill. At present, generally speaking, the old people went to the public hospitals. The chief indictment against the hospitals was that they were not made attractive. The authorities ought to start to build decent houses away from the taint of the poor-house for the old people to live in, then they would go in and there would be no need to exercise compulsory powers.

The Bill was read a second time, and committed to a Standing Committee.

Miners and Silicosis

In the House of Commons on March 29th, on the motion for the adjournment for the Easter recess,

Mr. D. GRENFELL called attention to the wide prevalence of silicosis. He said that an inquiry was held in 1925 by the Mines Department. A report was made to the Department confirming the belief that silicosis in this country was identifiable with miners' phthisis, which had caused such ravages among the South African miners and for which special legislation was provided. Since 1925 there had been investigations and references to departmental committees, but it was not until 1929 that a regulation was issued by the Home Office acknowledging the liability of employers to pay compensation to the victims of this disease. Silicosis was spreading to an alarming extent in the mining industry. The Secretary for Mines must have been surprised at the result of the inquiries made at his (Mr. Grenfell's) instance a short time ago.

It was reported that during a certain period there had been certified in the mines of this country 400 people so disabled as readily to obtain certification. He believed that that figure represented only a small part of the incidence of the disease. He dreaded to estimate the number of people who would become certified year after year as time went on. He urged the Home Secretary to pursue those inquiries which were taking place by the medical staff of his department working in collaboration with a special medical man appointed by the Mines Department. He

would like the two Ministers to expedite those investigations with all possible speed. Silica, he was convinced, was not the only mineral which was responsible. There was in the silicious rocks an element called sericite which played a very large part in the production of this disease.

In certain parts of the coalfields the presence of silica and the percentage of it did not account for such widespread prevalence of the disease as in other areas. For example, the figures given by the Inspector of Mines showed that of 424 cases in the whole of Great Britain 386 had been certified in South Wales; that was to say that in one coalfield, where there was 25 per cent. of the mining population, 80 per cent. of the silicosis cases were found. The incidence was higher in certain parts of South Wales than over the whole coalfield on an average. There were special areas where the incidence was exceptionally high, and that could not be explained by varying degrees of contamination with silica, but must be ascribed to some other cause.

Not only was he urging that these investigations should be actively pursued, but no time should be lost in adopting preventive measures. Medical science was quite helpless in this matter. No medical treatment could help these people who had contracted the disease or relieve their condition in the slightest. He would like to see a "safety first" campaign directed to known preventive measures. He was not satisfied that any effective dust-trap had yet been invented. Nor did he think that an effective respirator had been produced which could be made portable and which people could be obliged to wear.

Mr. GRENFELL said he would like to make these preventive measures automatic—not merely dust-proof, but fool-proof—with no possibility of pollution of the air taking place; and the only way that that could be done was to lay the dust at the spot where it was made before it emerged into the atmosphere. To do that effectively a system of wet drilling was the only one which commended itself to him, and there was no reason that he was aware of why an Order should not be made by the Secretary for Mines. He believed that hundreds of lives would be saved if wet drilling were compulsorily imposed.

After further debate, Sir JOHN GILMOUR (Home Secretary) said that one of the great administrative difficulties in dealing with the question was to find absolutely sure and certain ground upon which they could work. Opinions were held by some that the use of water in dealing with drills or laying dust was considered to be a solution. If it was as simple as that they could feel that they could at once take a step forward, but he was informed by those who had studied the problem that while there might be much to be said for using part of this system it was really not conclusive. He thought it was true that they were only working on the fringe of these problems, but he understood that the scientists had been working with a common purpose and with all possible expedition to try, if possible, to improve matters.

He understood, for instance, that there was a mask or respirator which shortly would be available for trial. As to the question of compulsion, they all knew the difficulties of getting a workman unaccustomed to these appliances to make use of them consistently It was necessary that the beneficial results of such appliances should be explained to the workmen. The Home Office realised that there were difficulties in the width of the source from which infection could come. He understood from those who had investigated the matter that while it was true that sericite was found in certain cases to have deleterious results it had never been established that any case had been proved in which at the same time silica had not been present. If he was right, while sericite might be a contributory cause of the disease, it was not a primary cause. He could assure the House that the Home Office and the Ministry of Mines were endeavouring to investigate the problem. Undoubtedly better ventilation in the mines was of immense importance. In regard to the problem of dust in mines, methods for limiting the range of the explosion were being investigated from all practical sides. If there was anything which could be done to limit the period of time within which it was possible to decide whether compensation was payable he would look into it with the greatest sympathy. Although knowledge of this problem was increasing, and more people might be coming into the arena to whom they could apply for help, the fact remained that this question could only be decided by those who were really conversant with the problem.

The Government, Sir John Gilmour concluded, were at present in communication with the mine owners upon this problem and were actively discussing the aspects—some of them new aspects—upon which quite clearly there were division of opinion on which science had not yet definitely come to a conclusion. He hoped that perhaps at a later stage in the session he might be in a position to say something further.

HOUSE OF COMMONS

TUESDAY, MARCH 27TH

State-aided Houses

Mr. KIRKWOOD asked the Secretary of State for Scotland how many State-aided houses were under construction in Scotland in March, 1933; the number under construction at present; and what was the cause of the decline.—Mr. SKELTON, Under-Secretary of State for Scotland, replied: The number of State-assisted houses under construction by local authorities and private enterprise in Scotland at March 31st, 1933, was 23,503. Figures for March are not yet available. For purposes of comparison I give figures for February of 1933 and 1934. These were 22,315 and 16,446 respectively. With regard to the second part of the question, the hon. Member will recollect that local authorities are at present concentrating upon programmes for slum clearance. These are not sufficiently advanced to be reflected in the houses under construction at Feb. 28th, but the tenders approved for new construction are now showing the effect of this activity, the number of tenders approved for February, 1934, under the Act of 1930, being 1122 compared with 334 in February, 1933.

Shortage of Water-supplies in Scotland

Mr. KIRKWOOD asked the Secretary of State for Scotland how many local authorities in Scotland had reported a shortage of water-supplies; how many villages had no proper supply, even apart from the drought; what action the Government proposed to ensure a supply for all parts of Scotland; and if he was aware that in the vicinity of Loch Katrine there were hamlets and villages which had been short of water-supplies since last summer.—Mr. SKELTON replied: As regards the first two parts of the question, of the local authorities who have so far replied to the inquiry made by the Department of Health in January last, 50 town councils and 9 county councils have reported a shortage of water in their areas during 1933. The replies from the 9 county councils referred to shortages in 65 special water-supply districts, and 43 villages without publicly owned supplies. As regards the third part, the department propose, immediately the Bill at present under consideration in another place is passed, to invite applications from local authorities who desire to participate in the grant to be made available for the improvement of rural water-supplies. As already stated in the House, the Government have under consideration further steps for dealing with an emergency due to the drought should circumstances so require. As regards the last part of the question, I am informed that the only village in the vicinity of Loch Katrine which has been short of water since last summer is Brig o' Turk, and that this case is at present receiving the attention of the county council of Perth.

Medical and Nursing Services in Scottish Islands

Mr. T. B. W. RAMSAY asked the Secretary of State for Scotland if he was aware that there were no hospitals, nursing, or maternity homes in the islands of Harris, North Uist, Benbecula, and Barra, or the smaller islands adjacent thereto, with the exception of a casual sick house in Harris; if he was aware that the medical services for the said islands were performed by visiting doctors and nurses; and what provision was made for sudden and serious illnesses, accidents, and maternity cases in these islands.—Mr. SKELTON replied: The answer to the first part of the question is in the affirmative. The medical and nursing services are provided by doctors and nurses actually resident on the islands named. As regards the last part of the question, arrangements are made wherever practicable for the removal of patients from Harris to the hospital at Stornoway, and from the other islands named either to Oban or Glasgow. Cases from Benbecula are sometimes treated in the private hospital on South Uist. The doctor at Benbecula was specially selected for

appointment because of his surgical knowledge and experience. In urgent cases, as an alternative to the removal of the patient, the surgeon from Stornoway, accompanied if need be by a nurse, may travel to his home.

Small-pox at Blackburn

Mr. GROVES asked the Minister of Health whether any of the Blackburn small-pox patients had been vaccinated before removal to hospital with small-pox; and, if so, how many days before such removal was the vaccination performed in each case.—Sir HILTON YOUNG replied: Five patients were vaccinated shortly before removal to hospital. Two of these were vaccinated during the incubation period of the disease six and ten days respectively before removal. Three were vaccinated after the illness had begun—one on the day of removal, one the day before removal, and the third four days before removal.

Medical Examination of School-children

Mr. GROVES asked the Parliamentary Secretary to the Board of Education whether any regulations existed that required the presence of a female nurse during the medical examination of school-children.—Mr. RAMSBOTHAM replied: The Board of Education have not made any regulation requiring the presence of a nurse during the medical examination of school-children, but it is the general practice for a school nurse or some other woman helper to be present.

Sickness Benefit and Housework

Mr. PARKINSON asked the Minister of Health if he had authorised the decision that when an insured woman, who was in receipt of national health insurance benefits, was certified by a medical officer as being able to do housework though unable to follow her usual occupation, her benefits should cease, even though she intended to resume her own occupation as soon as her health would permit.—Sir HILTON YOUNG replied: There is no general decision that an insured woman who, though unable to follow her usual occupation, is able to do housework, is to be treated as not entitled to sickness or disablement benefit. An approved society would not ordinarily regard such a woman as disentitled to benefit pending her early return to her normal employment, but in the case of a woman who is the domestic head of a household and for whom, accordingly, the performance of household duties is in the nature of an alternative to her industrial employment, fitness for the former as well as for the latter form of work would properly be taken into consideration. Societies have been informed that it is their duty to consider every such case on its merits, and any woman who is dissatisfied with the decision of her society is entitled to appeal in accordance with the rules of the society.

WEDNESDAY, MARCH 28TH

New Formulæ for Surgical Spirit

Miss HORSBRUGH asked the Secretary to the Treasury the reason for the withdrawal as from March 15th, 1934, of the formula permitted during the past years for the manufacture of the preparation of methylated spirit known as surgical spirit and the substitution of two new alternative formulæ.—Mr. HORE-BELISHA replied: The object was to achieve a still higher degree of unpalatability in the product.

THURSDAY, MARCH 29TH

Medical Examination of Motorists charged with being Drunk

Mr. ISAAC FOOT asked the Home Secretary if he had now been able to consider the remarks of Mr. Justice Swift at the recent Liverpool assizes as to the examination of persons charged with being intoxicated whilst driving motor-cars; and if he proposed to amend the existing practice relating to the examination of such persons by doctors called in by the police.—Sir J. GILMOUR replied: I have had this matter under consideration, but at the moment I am not in a position to make any statement.

Food Standards

Captain ERSKINE-BOLST asked the Minister of Health when the report of the departmental committee on food standards would be available.—Sir HILTON YOUNG replied: The report has just been presented to me, and I am giving instructions for its publication as soon as possible after Easter.

MEDICAL NEWS

Society of Apothecaries of London

At recent examinations the following were successful:—

Surgery.—A. J. L. Bolger, Univ. of Liverp.; J. L. Freer, Guy's Hosp.; J. C. Harvey, St. George's Hosp.; C. W. O'Donoghue, London Hosp.; F. D. Paterson, St. Mary's Hosp.; J. D. Taylor, Univ. of Manch.; and T. H. N. Whitehead, Univs. of Oxf. and Leeds.

Medicine.—A. J. L. Bolger, Univ. of Liverp.; A. C. E. Cole, Univ. of Camb. and St. Mary's Hosp.; R. Frankling, Guy's Hosp.; J. Lipschitz, Westminster Hosp.; B. C. M. Palmer, Univ. of Camb. and Guy's Hosp.; and T. H. N. Whitehead, Univs. of Oxf. and Leeds.

Forensic Medicine.—A. J. L. Bolger, Univ. of Liverp.; M. T. Curran, Univ. of Leeds; B. C. M. Palmer, Univ. of Camb. and Guy's Hosp.; H. Paroulakis, Univ. of Innsbruck and St. Mary's Hosp.; J. H. Playne, St. Mary's Hosp.; F. W. Treadwell, Univ. of Birm.; and T. H. N. Whitehead, Univs. of Oxf. and Leeds.

Midwifery.—A. J. L. Bolger, Univ. of Liverp.; R. N. Crossley, Univ. of Manch.; M. T. Curran, Univ. of Leeds; B. Dayal, Univ. of Durham; J. H. Playne, St. Mary's Hosp.; and T. H. N. Whitehead, Univs. of Oxf. and Leeds.

The following candidates, having completed the final examination, are granted the diploma of the society entitling them to practise medicine, surgery, and midwifery: A. J. L. Bolger, A. C. E. Cole, B. Dayal, R. Frankling, J. L. Freer, J. C. Harvey, J. Lipschitz, B. C. M. Palmer, J. D. Taylor, and T. H. N. Whitehead.

Honours for Sir H. Wellcome

The American Pharmaceutical Association has awarded its Remington medal, which is conferred for distinguished service to pharmacy, to Sir Henry Wellcome, F.R.S., founder of the Wellcome Research Institution and head of Burroughs Wellcome and Co. Apart from the numerous laboratories of the establishments of his firm, Sir Henry has established a number of research laboratories and museums which are coördinated as the Wellcome Research Institution. The new building of this institution occupies a site in the Euston-road, London.

The President of the French Republic has conferred upon Sir Henry the Cross of Chevalier of the Legion of Honour.

Royal College of Surgeons of Edinburgh

At recent examinations the following candidates were successful:—

L.D.S.

L. B. Corner, W. R. Weatherston, T. H. Thompson, R. J. E. Derwent, W. H. Charlton, R. O. Walker, A. E. Thompson, A. V. Robson, J. H. Quin, Frederick Gilhespie, W. R. D. Boyd, and G. A. McC. Durran.

Charing Cross Hospital Nurses' Hostel

It has been decided to complete the original scheme for this hostel at Haverstock Hill at a cost of £30,000. It will then be possible to release much space in the hospital for paying patients. By the generosity of the Daimler Company the nurses are carried to and fro in two large motor coaches.

University of Liverpool

On Friday, May 11th, the University will celebrate the centenary of the incorporation of its medical school. It is proposed to confer the honorary degree of D.Sc. on Dr. Henry Dean, professor of pathology in the University of Cambridge, and Master of Trinity Hall; Sir Thomas Lewis, F.R.S., physician to University College Hospital, London; Mrs. May Mellanby, investigator for the Medical Research Council; and Mr. Wilfred Trotter, F.R.S., surgeon to University College Hospital, London. The honorary degree of LL.D. will be conferred on Prof. William Blair-Bell, who held the chair of obstetrics and gynæcology in the University from 1921 to 1931, and was first president of the British College of Obstetricians and Gynæcologists; Prof. Henry Briggs, the previous holder of the chair (1898–1921); Dr. H. R. Hurter, past president of the Liverpool Medical Institution; and Dr. W. S. Paget-Tomlinson, lately chairman of the public health committee of Westmorland.

Gift for Radiology at Middlesex Hospital

Mr. E. W. Meyerstein has given £30,000 for the establishment of a new department of radiology.

University of Glasgow

At a graduation ceremony to be held on June 20th the honorary degree of LL.D. will be conferred on Dr. René Leriche, professor of clinical surgery in the University of Strasbourg.

German Radiological Society

The twenty-fifth congress of this society will take place at Baden-Baden from April 14th to 16th. Particulars may be had from Dr. Kloiber, Röntgenabteilung des Städtischen Krankenhauses, Baden-Baden.

Surgical Treatment of Tuberculosis

At the annual meeting last week of the governors of the Brompton Hospital for Consumption, Lord Derby said that whereas 12 years ago there were 66 cases of surgical treatment and one visiting surgeon, the hospital now has two surgeons and two assistant surgeons on the staff, and the surgical operations last year reached the record total of 1122. The daily average of occupied beds was 464.

Westminster Hospital Appeal

Westminster Hospital has succeeded in raising within five months the £100,000 required to secure the site at St. John's-gardens, Millbank, on which a new hospital is to be built at a cost of £700,000. Two large donations lately received which have helped to bring the fund to its present total of nearly £107,000 are £10,000 voted by the Middlesex county council and £5000 from the James Gardiner trust. The other half of the sum needed to buy the site will, it is hoped, be obtained by selling the ground occupied by the present building.

Soho-square Hospital for Women

The 1410 in-patients treated last year were the lowest number since 1929, and consequently the average cost per patient increased considerably. The number of new out-patients has also fallen, but the attendances have increased owing to the opening of the new clinic for the special treatment of certain cases.

A Waiting-list at Belfast

On Dec. 31st, 1933, the waiting-list at the Royal Victoria Hospital, Belfast, numbered 1025. There were 6285 admissions, the highest on record, but the average stay of 21·9 days was the shortest yet recorded, being a reduction of 2·5 days compared with 1932. Last year the hospital spent £1590 upon motor accident patients, of which only £374 had been recovered. At the end of the year there were, however, still 127 claims outstanding. The daily average number of beds occupied was 400.

Hospital Treatment for the Middle Class

After long negotiations a scheme has been agreed to by the Hospital Service Association and the Hospital Staffs Association at Liverpool whereby hospital treatment is assured to people of the middle class. For a payment of 1*s.* per week, contributors with no dependents, whose annual income does not exceed £400, or with one dependent £500, or with more than one dependent £600, will be entitled to first-class hospital treatment, including necessary surgical and medical attention whilst an in-patient. Dependents of a person whose income comes within these limits also are entitled to benefit. A minimum membership of 10,000 is anticipated.

Royal Northern Hospital

At the recent annual meeting of the Royal Northern Group of Hospitals it was stated that the total complement of beds is 466, of which 43 have been closed for the last two years for lack of means. Last year the casualty department, which is the Islington war memorial, received 17,475 patients, a large number of them motor accident cases. Patients, including those in the St. David's pay-bed wing, paid a total of £54,346. It is hoped that the nurses' home, begun last year, will speedily be completed to accommodate the 156 nurses who are in the main building of the group. The debt now amounts to £139,000, of which £73,000 is on account of the land and buildings of the whole group; their cost has been £433,000.

Medical Diary

SOCIETIES

ROYAL SOCIETY OF MEDICINE, 1, Wimpole-street, W.
MONDAY, April 9th.
United Services. 4.30 P.M. Annual General Meeting. Surg.-Commander J. G. Danson: The Symptom of Vertigo.

NORTH LONDON MEDICAL AND CHIRURGICAL SOCIETY, Royal Northern Hospital, Holloway-road, N.
THURSDAY, April 12th.—9 P.M., Dr. E. G. B. Calvert: Clinical Demonstration.

HUNTERIAN SOCIETY.
MONDAY, April 9th.—7.15 P.M. (at Simpson's Restaurant, Cheapside), Annual General Meeting followed by an Address by Sir Frederick Hobday on the Debt Veterinary Science owes to John Hunter. (Lantern Slides and Cinema Films.)

SOUTH-WEST LONDON MEDICAL SOCIETY, Bolingbroke Hospital, Wandsworth.
WEDNESDAY, April 11th.—9 P.M., Dr. T. C. Hunt: Recent Advances in Treatment.

MEDICAL SOCIETY OF INDIVIDUAL PSYCHOLOGY, 11, Chandos-street, W.
THURSDAY, April 12th.—8.30 P.M., Dr. H. C. Squires: Individual Psychology and the European in the Tropics.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY, Stepney Green, E.
THURSDAY, April 12th.—3 P.M., Clinical Meeting.

SOCIETY FOR THE STUDY OF INEBRIETY, 11, Chandos-street, W.
TUESDAY, April 10th.—4 P.M., Sir Humphry Rolleston: Aims and Work of the Society during the 50 years of its existence.

LECTURES, ADDRESSES, DEMONSTRATIONS, &c.

FELLOWSHIP OF MEDICINE AND POST-GRADUATE MEDICAL ASSOCIATION, 1, Wimpole-street, London, W.
MONDAY, April 9th, to SUNDAY, April 15th.—ST. MARK'S HOSPITAL, City-road, E.C. Course in Proctology. All day.—INFANTS HOSPITAL, Vincent-square, S.W. Course in Infants' Diseases. Afternoons.—BRITISH RED CROSS CLINIC FOR RHEUMATISM, Peto-place, N.W. Tues. and Thurs., at 8 P.M. Course in Rheumatism.—SOUTHEND-ON-SEA GENERAL HOSPITAL. Week-end Course in Medicine and Surgery. Sat. and Sund. All day.—MEDICAL SOCIETY OF LONDON, 11, Chandos-street, Cavendish-square, W. Lecture-demonstration by Dr. A. E. Clark-Kennedy on Shortness of Breath. Tues., at 2.30 P.M.—NATIONAL TEMPERANCE HOSPITAL, Hampstead-road, N.W. A Demonstration of Surgical Cases, by Mr. A. E. Mortimer Woolf, on Sat., at 3 P.M.—WEST END HOSPITAL FOR NERVOUS DISEASES, In-patient Department, Gloucester-gate, N.W. Demonstration on the Fundus Oculi, by Mr. R. Lindsay Rea, on Wed., at 8.30 P.M. (Specially suitable for M.R.C.P. candidates.)—MEDICAL SOCIETY OF LONDON, 11, Chandos-street, Cavendish-square, W. Lectures by Dr. Philip Ellman on Wed., at 8.30 P.M. Pulmonary Tuberculosis (1), and Frid., Pulmonary Tuberculosis (2).—PANEL OF TEACHERS. Individual Clinics in various branches of Medicine and Surgery are available daily by arrangement with the Fellowship of Medicine. Courses of instruction, clinics, lectures, &c., arranged by the Fellowship of Medicine, are open only to Members and Associates.

ROYAL NORTHERN HOSPITAL, Holloway-road, N.
TUESDAY, April 10th.—3.15 P.M., Mr. Eric I. Lloyd: The Surgery of Poliomyelitis. (Lecture-demonstration.)

CENTRAL LONDON THROAT, NOSE, AND EAR HOSPITAL, Gray's Inn-road, W.C.
FRIDAY, April 13th.—4 P.M., Mr. A. Lowndes Yates: Emergency Operations in the Throat, Nose, and Ear.

UNIVERSITY OF BIRMINGHAM.
TUESDAY, April 10th.—3.30 to 5 P.M. (at the General Hospital), Mr. F. A. R. Stammers: The Newer Surgery of the Sympathetic Nervous System. Demonstration of cases.
FRIDAY.—3.30 to 5 P.M. (at the Queen's Hospital), Dr. G. Eden: Demonstration of Medical Cases.

ANCOATS HOSPITAL, Ancoats, Manchester (Post-graduate Lecture).
THURSDAY, April 12th.—4.15 P.M., Mr. P. G. McEvedy: Diseases of the Salivary Glands.

LEEDS GENERAL INFIRMARY.
TUESDAY, April 10th.—3.30 P.M., Mr. Black: Demonstration of Ophthalmic Cases.

MANCHESTER ROYAL INFIRMARY.
TUESDAY, April 10th.—4.15 P.M., Mr. W. H. Hey: The Present Position of Treatment of Cancer of the Breast.
FRIDAY.—4.15 P.M., Dr. W. Brockbank: Demonstration of Medical Cases.

SALFORD ROYAL HOSPITAL.
FRIDAY, April 13th.—4.15 P.M., Mr. R. Ollerenshaw: Surgical Treatment of Paralysis. (Cinematograph Demonstration.)

GLASGOW POST-GRADUATE LECTURES.
WEDNESDAY, April 11th.—4.15 P.M. (at the Western Infirmary), Dr. J. G. Macgregor-Robertson: Male Venereal Diseases.

NOTES, COMMENTS, AND ABSTRACTS

THE MARYLEBONE RHEUMATISM CLINIC

THE fourth year of the British Red Cross Society's clinic for rheumatism at Peto-place, Marylebone-road, has shown the staff the kind of clinical material that may be expected at an out-patient department of this kind. According to the classification now approved by the visiting physicians the percentage of patients was as follows:—

Patients Showing Some Form of Rheumatism

	Group A. Articular.	*Group B.* Non-articular.
1. Infective—		
(*a*) Non-specific	15·5	11·4
(*b*) Specific	1·8	1·3
2. Traumatic	2·8	2·0
3. Degenerative—		
(*a*) Senile (osteo-arthritis)	17·0	0·3
(*b*) Climacteric	5·1	1·2
4. Metabolic—		
(*a*) Gout	2·2	0·3
(*b*) Rheumatoid	4·3	0·04
(*c*) Other Metabolic	2·8	2·3
5. Unclassified	2·1	17·3
	53·6	36·1
Group C.—Patients suffering from some sequel of rheumatic fever		2·3
Group D.—Patients suffering from non-rheumatic conditions		8·0

There has been little variation in the relative percentages of the main groups for the past three years. A large number of patients suffering from some manifestation of rheumatism had, in addition, some associated non-rheumatic condition (but are not included in Group D).

Any attempt to assess the gross results of treatment must, in the medical board's opinion, be accepted with a certain amount of reserve, since there are so many factors that modify interpretation and deduction. The stage of the disease at which the patient comes up for treatment, the type of the rheumatic manifestation, the economic factor, the nature of the patient's occupation, the ability of the patient to take full advantage of the resources available for treatment, the presence of any associated non-rheumatic disease, all tend to alter and detract from the value of any figures that may be quoted. Bearing all these facts in mind, the following figures represent the results of the investigation into the effect of treatment on the 957 men and 1615 women who were discharged from the clinic during 1933. Of these 196 men and 419 women did not complete their treatment; 43 men and 54 women were discharged on account of intercurrent disease. Of the remaining 718 men and 1142 women:—

—	Men.	Women.	Men and women.
	Per cent.		
Cured	26·0	13·2	18·3
Considerably improved	25·9	27·6	26·8
Definitely "	32·5	36·6	35·0
Slightly "	2·2	3·8	3·2
Unchanged	12·1	17·8	15·6
Worse	1·3	1·0	1·1

This year, as last, the percentage of men discharged as cured is almost double that of the women. The explanation given is that a larger proportion of men attending the clinic were suffering from some non-articular form of rheumatism, and that men, being usually the chief wage-earner of the family, were more likely to present themselves for treatment early, owing to the serious economic results of prolonged disability.

During the year the ten beds allocated for in-patient treatment to the clinic by the London County Council have been transferred from St. Charles' Hospital to St. Stephen's. The report emphasises the need for facilities to be provided for in-patient treatment under their supervision at a site near to the clinic, where any special or detailed investigations, as well as any form of physical or other type of treatment can be carried out that would be impracticable in an out-patient department. The lack of these facilities is proving a handicap to the work.

The need for continued research is being borne in mind. There are several clinical assistants whose time is now almost entirely taken up with routine examinations and investigations. Some grant of money would be required if new investigations are to be made, and the appointment of one or more full-time research workers would have to be considered. Directions of past and present work are these:—

An investigation of the vasomotor changes in rheumatoid arthritis.

The effect of vaccine treatment of rheumatism.

A comparison of the clinical results of treatment by autogenous, stock, and non-specific vaccines.

The value of acetylcholine injections in the treatment of rheumatism.

The assessment of the climatic factors in the rheumatic diseases.

An investigation of the types of arthritis occurring at the menopause.

The value of histamine ionisation in the treatment of rheumatism.

The treatment of arthritis by pelvic diathermy.

A comparison of the results obtained by different physical treatments.

Differential diagnosis of chronic arthritis affecting the hip-joint.

The value of the sedimentation-rate.

The use of gold salts in the treatment of arthritis.

Periodic demonstrations are given by members of the visiting staff, and regular courses of post-graduate lectures under the auspices of the Fellowship of Medicine. Lectures in medical hydrology have also been delivered to members of the Chartered Society. Each visiting physician has a senior as well as several junior clinical assistants; the appointment enables qualified practitioners anxious to gain experience of the physiotherapeutic and other methods employed in the treatment of rheumatism.

LEAD AND WATER

ALTHOUGH poisoning due to the use of lead pipes for conveying water has been recognised since Roman times it still finds occasional victims—as, for instance, in the Scottish outbreak reported in our columns last year.[1] It is, therefore, cause for satisfaction that the Water Pollution Research Board is devoting attention to this source of danger. A summary of existing knowledge of the subject has just been issued by the Board, apparently as a preliminary to research at the Chemical Research Laboratory, Teddington, and this summary,[2] which has been prepared by Mr. H. Ingleson, D.Phil., itself illustrates the need for investigation under precisely defined conditions.

On the physiological or pathological side it seems that people vary greatly in their susceptibility to lead poisoning and that the classical symptoms associated with industrial poisoning are not necessarily to be expected when the lead is taken in drinking water. At the outset Ingleson quotes Wynne, who thinks it possible that "rheumatic" cases which derive temporary benefit at watering-places and spas may be cases of undetected plumbism arising from small quantities of lead habitually ingested with water. Since the urine and fæces of "normal" subjects contain appreciable quantities of lead it is difficult to say when lead ingestion begins to be harmful. Various authorities give widely differing amounts of lead as conferring dangerous properties on water, for whilst Wright, Sappington,

[1] THE LANCET, 1933, ii., 374 and 1156.

[2] Department of Scientific and Industrial Research, Water Pollution Research, Technical Paper No. 4, The Action of Water on Lead with special reference to the Supply of Drinking Water, Summary of Existing Knowledge. By H. Ingleson, M.A., D.Phil. London: H.M. Stationery Office. 1934. 2*s*.

and Rantoul consider that as little as 0·3 part per million has caused poisoning, and most American workers fix this as a limit, Thresh, Beale, and Suckling would allow up to 0·5 part and A. Smith has found that 1·44 part is "not dangerous to some people." It may be observed that some drink very little water, and that lead tends to be removed from solution (or quasi-solution) in the process of preparing tea or coffee.

Ingleson states that lead pipes are in use in Cordova which date from the Moorish occupation about A.D. 850 and other very old pipes are in use and have given rise to no toxic symptoms. It is usually stated that hard water attacks lead less than soft water, but though this seems in the main to be true, notable exceptions have been observed. It may be taken as certain that pure distilled water does not act on pure lead in the absence of oxygen. This was shown by Lambert and Cullis, who also found that whilst lead which had been in contact with water for 12 months was tarnished only slowly when oxygen was admitted, in some cases lead which had been in water for only a few days after it (the lead) had been distilled tarnished rapidly when oxygen was admitted. In fact the amount of attack seems to depend on the state of the lead or on the metals with which it is alloyed as well as on the impurities of the water.

NEW PREPARATIONS

SOMNACETIN (Dr. R. and Dr. O. Weil, Frankfort-on-Main. Agent: Francis O. Rudloph-Riddell, Sentinel House, Southampton-row, London, W.C.).—This is a hypnotic of the barbituric group concerning whose utility articles have appeared in the German press for several years. It is a Sodium-diethyl-barbitone-Phenacetin-Codeine combination, and the literature confirms what might be expected of it therapeutically. We note that several of the articles give warning of the risks that may be incurred in taking it, but there appears to be no such caution issued with the various preparations—ampoules, tablets, capsules, drops, and suppositories. These are put on the market in convenient form and neatly packed, and the preparation has behind it useful authority as hypnotic and sedative.

MENFORMON (Organon Laboratories, 1, Gordon-square, London, W.C.).—This œstrogenic hormone is put up in two forms, an oily solution where each 1 c.cm. contains 10,000 international units and a watery solution where each 1 c.cm. contains 1000 international units. The biological standardisation has been carried out in the laboratories of the company at Oss, Holland, by Prof. E. Laqueur, director of the department of pharmacology and therapeutics, Amsterdam. The aqueous solution is stated to be the strongest that can be made without precipitation and is easy to inject.

Births, Marriages, and Deaths

BIRTHS

BAILEY.—On March 24th, at Bentinck-street, the wife of Dr. C. P. Bailey, The Chantry, Ingatestone, Essex, of a daughter.

DAVIDSON.—On March 24th, the wife of A. Whyte Davidson, F.R.C.S.E., Christchurch, Hants, of a daughter.

EARLAM.—On March 26th, the wife of Francis Earlam, M.D., Quendale, Mossley Hill, Liverpool 18, of a son.

POWER.—On March 26th, at Hereford, the wife of R. Wood Power, F.R.C.S.I., of a son.

MARRIAGES

ABRAHAMS—LESSER.—On March 27th, Sidney Abrahams, M.D., of Grove Green-road, Leytonstone, to Marion Hilary, only daughter of Mr. and Mrs. Albert Lesser, of Brondesbury House, Willesden-lane, N.W.

CHEETHAM—BIRCH.—At Hope Church, Wigan, on April 2nd, J. W. Cheetham, M.D., to Marjorie Birch, M.B., Ch.B., only daughter of Mr. and Mrs. A. J. Birch, of Gidlow-lane, Wigan.

DEATHS

FERNIE.—On March 30th, at Stone, Staffordshire, John Firth Fernie, M.R.C.S., L.R.C.P., aged 61 years.

NIXON.—On March 24th, at Plympton House, Plympton, John Clarke Nixon, M.B., aged 63 years.

PARK.—On March 31st, George Williamson Park, M.B., C.M., B.Sc., of Abbotsford-crescent, Edinburgh, late of the Medical Department, Edinburgh Town Council.

N.B.—A fee of 7s. 6d. is charged for the insertion of Notices of Births, Marriages, and Deaths.

Appointments

RADFORD, M., M.D., B.S. Lond., has been appointed Medical Officer of Health for St. Pancras.

City of London Maternity Hospital: MOON, A. A., M.B. Syd., Senior Resident Medical Officer; GILBERT, B., M.B., B.S. Lond., Junior Resident Medical Officer.

Medical Referees under the Workmen's Compensation Act: BATT, R. E. A., M.B., B.Ch. Oxf. (Circuit 33, Bury St. Edmunds, &c.); DRINKWATER, S. W., M.B., Ch.B. Manch. (Circuit 23, Atherstone, &c.).

Vacancies

For further information refer to the advertisement columns

Aberdeen, City Fever Hospital.—Jun. Res. M.O. £100.

Albert Dock Hospital, Connaught-road, E.—Res. M.O. At rate of £110.

Birmingham and Midland Eye Hospital.—Res. Surg. O. £200.

Birmingham, Erdington House.—Second Asst. M.O. £650. Also Jun. Asst. M.O.'s. Each at rate of £200.

Brighton County Borough.—Sen. Res. Asst. M.O. £400.

Brighton Education Committee.—Asst. School M.O. and Asst. M.O.H. £500.

Brighton, Royal Sussex County Hospital.—Hon. Clin. Asst. to Ophth. Dept.

Bristol University.—Lecturer in Dental Mechanics.—£600–£700.

Cambridge, Addenbrooke's Hospital.—H.P. and H.S. to Spec. Depts. Each at rate of £130.

Canterbury, Kent and Canterbury Hospital.—H.S. At rate of £125.

Chester City Hospital.—Res. M.O. £400.

Croydon, Mayday Hospital.—Jun. Res. Asst. M.O. £300.

Eastbourne, Princess Alice Memorial Hospital.—Two Hon. Anæsthetists. Also Res. H.S. £150.

East Ham Memorial Hospital, Shrewsbury-road, E.—Res. M.O. £200.

Glasgow, Royal Samaritan Hospital for Women.—Asst. Radiologist.

Golden-square Throat, Nose and Ear Hospital, W.—H.S. £100.

Hampstead General and N.W. London Hospital, Haverstock Hill, N.W.—H.S. At rate of £100.

Harrogate Royal Bath Hospital.—Res. M.O. At rate of £156.

Hospital for Epilepsy and Paralysis, 4, Maida Vale, W.—Res. M.O., and H.P. At rate of £150 and £100 respectively.

Hospital for Sick Children, Great Ormond-street, W.C.—Res. M.O. Country Branch Hospital. £250.

Ilford, King George Hospital.—H.S. At rate of £100.

King's College Hospital, Denmark Hill, S.E.—Hon. Radiologist.

Leicester, County Sanatorium and Isolation Hospital, Markfield.—Res. M.O. £400.

Lord Mayor Treloar Cripples' Hospital and College, Alton, Hants.—Asst. Res. M.O. £150–£200.

Manchester, St. Mary's Hospitals.—Three H.S.'s to Spec. Depts. Each at rate of £50.

Margate, Royal Sea-Bathing Hospital.—Res. Asst. Med. Supt. £500.

Merthyr Tydfil Education Committee.—Asst. School M.O. £500.

Middlesbrough, North Riding Infirmary.—Cas. O. £150.

Middlesex Hospital, W.—Asst. Radiologist. £400.

Miller General Hospital, Greenwich-road, S.E.—Hon. Ophth. Surg. Also Hon. Asst. Radiologist.

Nelson Hospital, Merton, S.W.—Res. H.S. At rate of £100.

Nottingham General Hospital.—H.P. At rate of £150.

Preston County Borough.—Asst. School M.O. £500.

Preston, County Mental Hospital, Whittingham.—Deputy Med. Supt. £750.

Princess Elizabeth of York Hospital for Children, Shadwell, E.—H.P. and Cas. O. Each at rate of £125.

Queen Charlotte's Maternity Hospital, Marylebone-road, N.W.—Hon. Ear, Throat, and Nose Surgeon.

Reading, Royal Berkshire Hospital.—H.P., H.S., and Cas. O. Each at rate of £150.

Rochdale Infirmary and Dispensary.—Jun. H.S. £200.

Rotherham Hospital.—Cas. H.S. £150.

Royal College of Surgeons of England.—Examiners.

Royal Masonic Hospital, Ravenscourt-park, W.—Res. Surg. O. At rate of £250.

St. Thomas's Hospital, S.E.—Physician.

Samaritan Free Hospital for Women, Marylebone-road, N.W.—H.S. At rate of £100.

Smethwick County Borough.—Sen. Asst. M.O.H. £750.

Southampton, Royal South Hants and Southampton Hospital.—Hon. Clin. Asst. to Ear, Nose, and Throat Dept.

Southend-on-Sea General Hospital.—Cas. O. At rate of £100.

South London Hospital for Women, Clapham Common, S.W.—H.P. At rate of £100.

Southport General Infirmary.—Jun. H.S. £150.

Stafford, Staffordshire General Infirmary.—H.P. At rate of £150.

Swansea General and Eye Hospital.—H.P. At rate of £150.

West End Hospital for Nervous Diseases, Gloucester Gate, Regent's Park, N.W.—H.P. At rate of £150.

Western Opthalmic Hospital, Marylebone-road, N.W.—Sen. and Jun. Res. H.S.'s. At rate of £150 and £100 respectively.

Woodside Hospital, Woodside Avenue, Muswell Hill, N.—H.P. £100.

DONATIONS AND BEQUESTS.—Greenock Royal Infirmary and Larkfield Hospital will benefit by a legacy of £1000 which has been left by ex-Bailie John Alston, at one time chairman of directors, for the purpose of endowing a bed in memory of his sister, Miss Janet Hill Alston.